

1 agggagagagc agtgaccag agggctgtgc tgcctgccc gtagatggca  
51 ggcttggccc tgcagccagg cactgcccgt ctgtgctact cctgcaaagc  
101 ccaggtgagc aacgaggact gctgcagggt ggagaactgc acccagctgg  
151 gggagcagtg ctggaccgct cgcatccgct cagtggcct cctgaccgtc  
201 arcagcaaag gctgcagctt gaactgcgtg gatgactcac aggactacta  
251 cgtgggcaag aagaacatca cgtgctgtga caccgacttg tgcaacgcca  
301 gcggggccca tgcctgcag ccggctgccc ccattcctgc gctgctcct  
351 gcactcggcc tgcctgctctg gggacccggc cagctatagg ctctgggggg  
401 ccccgtgca gccacactg ggtgtgtgtc ccaggcctt tgtgccactc  
451 ctacagaac ctggcccagt gggagcctgt cctggctcct gaggcacatc  
501 ctaacgcaag ttgaccatg tatgtttgca cccctttcc cnaaccctg  
551 accttccat gggcctttc caggattccn accnggcaga tcagtttag  
601 tganacanat ccgctgcag atggccctc caacntttt tgttgnrtt  
651 tccatggccc agcattttc acccttaacc ctgtgttcag gcacttttc  
701 ccccaggaag ccttccctgc ccaccccat tatgaattga gccaggttg  
751 gtccgtggtg tccccgcac ccagcagggg acaggcaatc agggaggccc  
801 agtaagggct gtagatgagt ggactgagta gactggagg acagaggtg  
851 acgtgagttc ctgggagttt ccagagatgg ggcctggagg cctggaggaa  
901 ggggccaggc ctacacattg tggggnccc gaatggcagc ctgagcacag  
951 cgtaggccct taataaacac ctgtggata agcc222222 22222222

FIGURE 1A

[illegible]



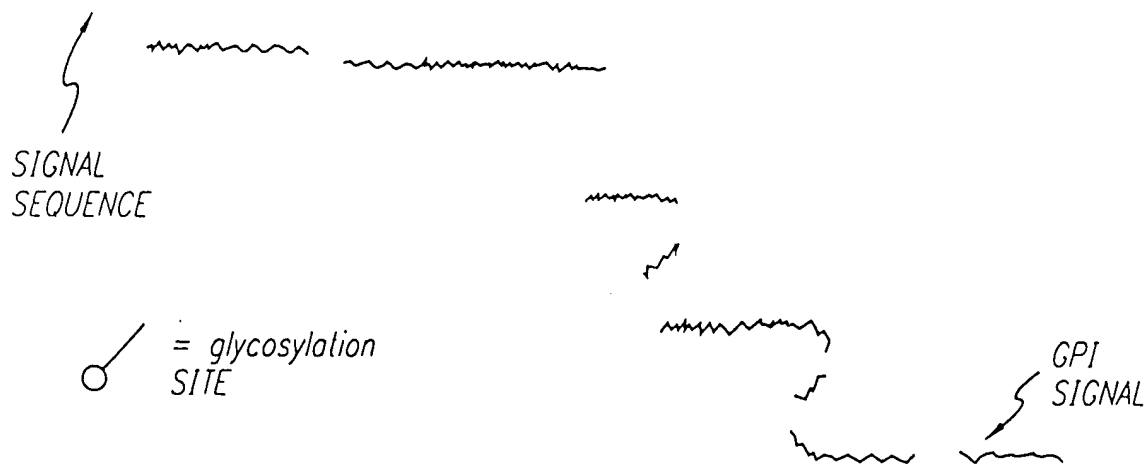
660020300000

1 M K I E T P V T T A A A L L G V S R A S S hSCA-2  
1 M K A V L L L A L L M A G P A L O P G T A hPSCA  
1 M K T V L S L L L A T Y T A L H P G A A mPSCA  
  
21 L M C F S C L N O K S N L Y C E K P T I  
21 L L C Y S C K A Q V S N S D C L Q V E N  
21 L Q C Y S C T A Q H N N R D C L N V Q N  
  
41 C S D Q O N Y C V T V S A S A G I G N L  
41 C T O L G E Q C W T A R I R A V G L L T  
41 C S L D Q H S C F T S R L R A I G L V T  
  
61 V T F G H S L S K T C S P A C P I P E G  
61 U - - - - I S K G C S L N C V D D S Q  
61 V - - - - I S K G C S S Q C E D D S E  
  
81 V N V G V A S M G I S C C Q S F L C N F  
76 D Y Y V G K K - N L T C C D T D L C N A  
76 N Y Y L G K K - N L T C C Y S D L C N V  
  
101 S A A D G G L R A S V T T T G A G L L L  
95 S G A A A L O P A A A L L A L L P A E G  
95 N G A A T L K P P T T L G L L T V L C S  
  
121 S L T P A L L R F G P  
115 L L L W G P G O L - -  
115 L L L W G S S R L - -

FIGURE 3

The image displays seven distinct horizontal tracks, each representing a different type of waveform or signal. From top to bottom, the tracks are: a flat line, a wavy line, a jagged line, a square wave, a complex stepped waveform, a trapezoidal waveform, and a series of sharp spikes.

FIGURE 4



**FIGURE 5**

Western Blot  
 Superoxide 8097 Hb  
 Normal tissue  
 1hr exp

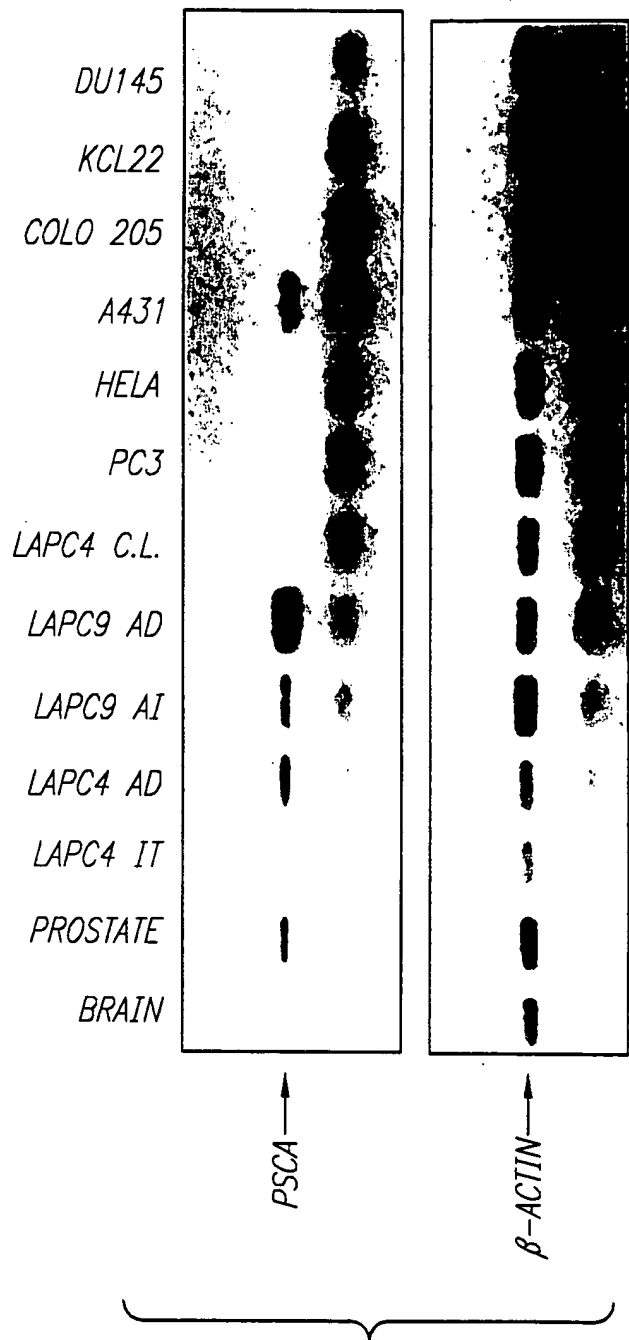
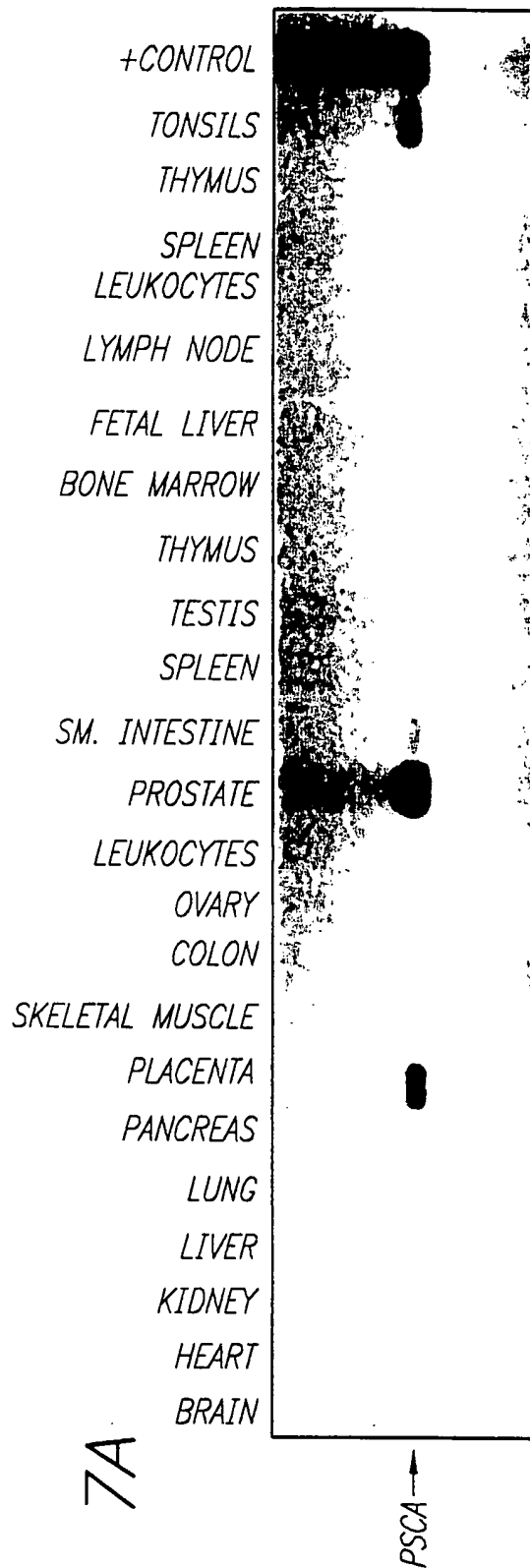
168  
 1:100

prostate (Humer)  
 prostate (Baker)  
 prostate (deK)  
 Bladder (Humer)  
 Bladder (deK)  
 Bladder (Rob)  
 Kidney (NABO)  
 Kidney (WU2)  
 Testis  
 Sm. Intest.

LA PC9

FIGURE 6

60020"926660





66020336260

Legend:  untranslated region of PSCA


 translated region of PSCA

FIG. 8A

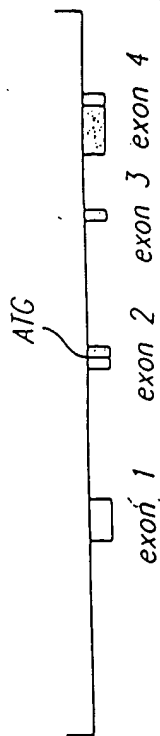


FIG. 8B

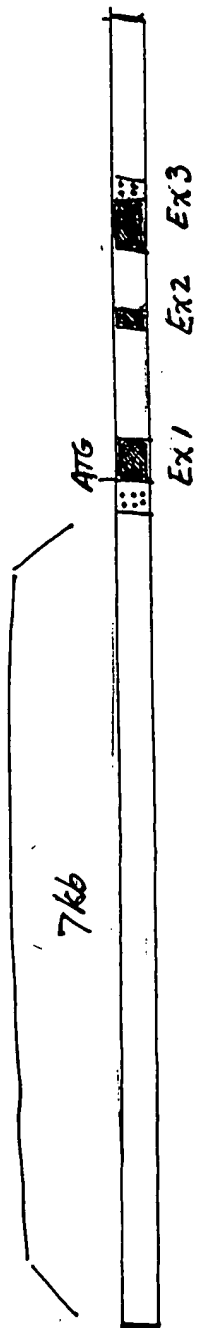
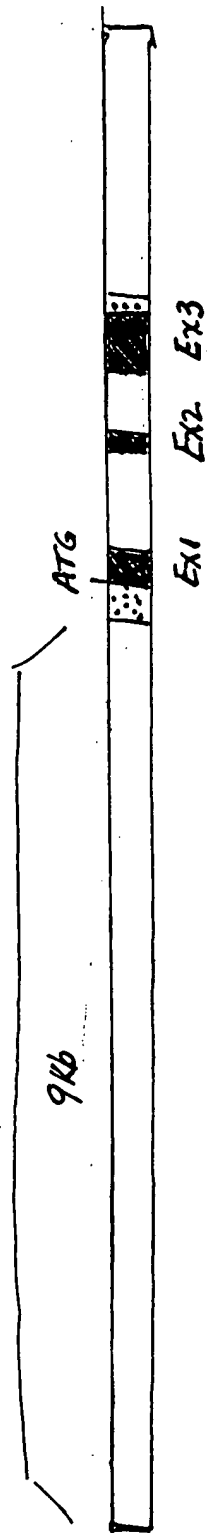


FIG. 8C



transcribed PSCA

FIGURE 8

transcribed PSCA

PSCA / PSA Expression in Benign  
Prostate vs. Prostate Cancer Xenograft

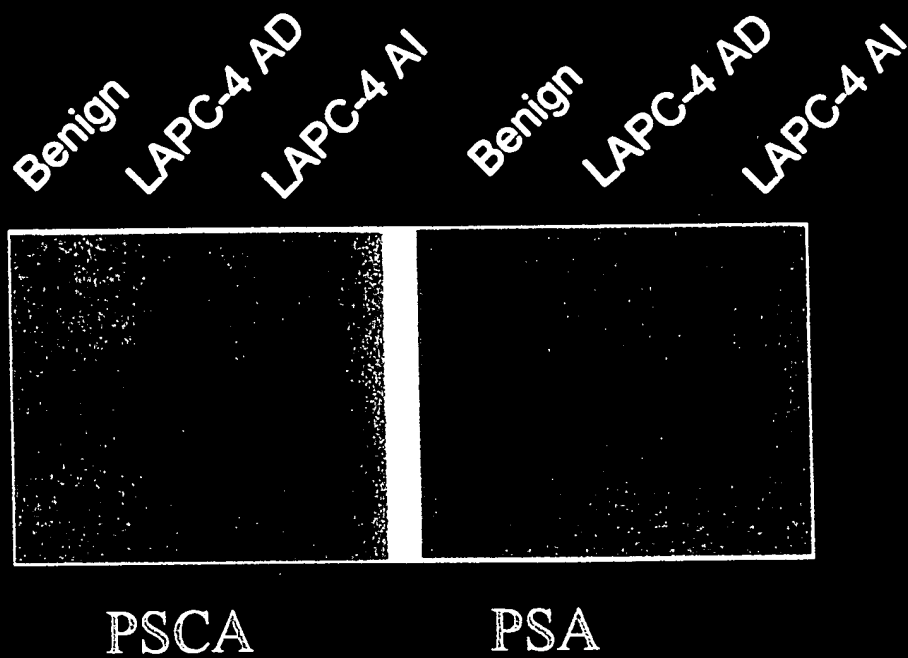
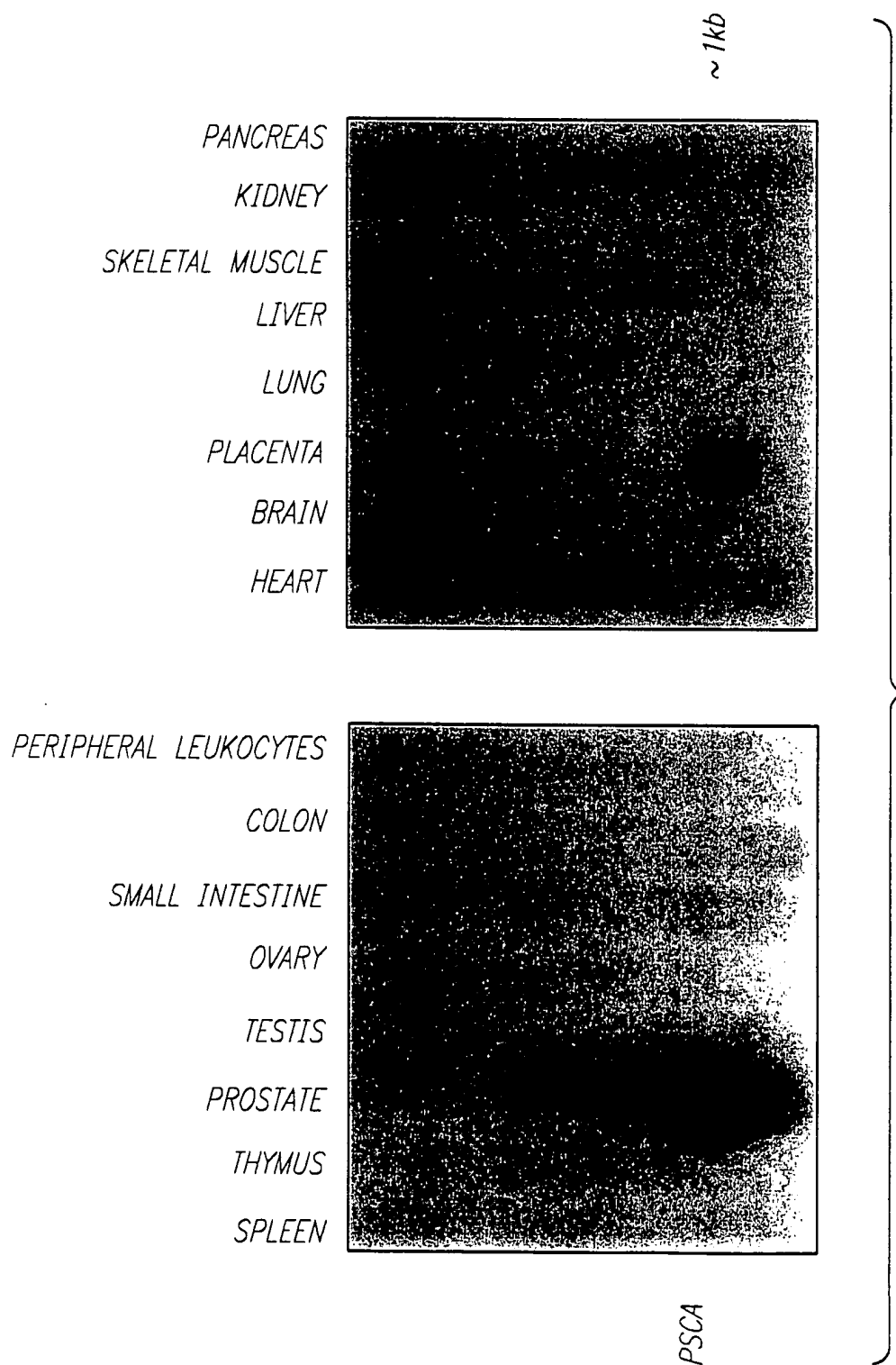


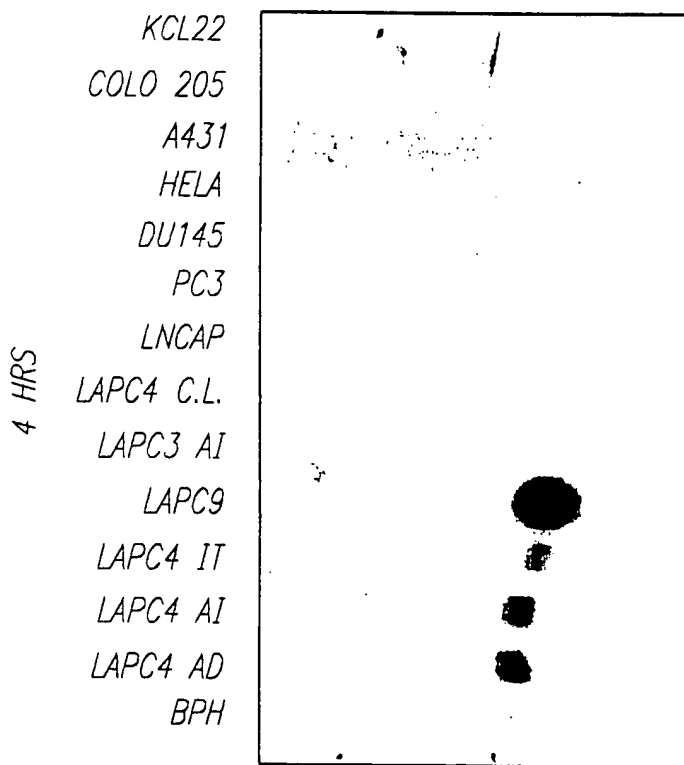
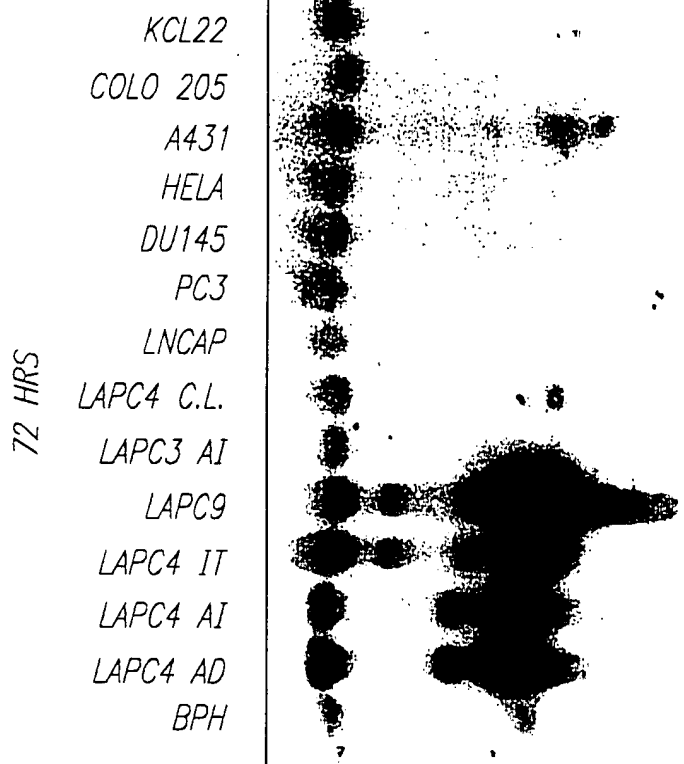
FIGURE 9A

66040-326360



*FIG. 9B*

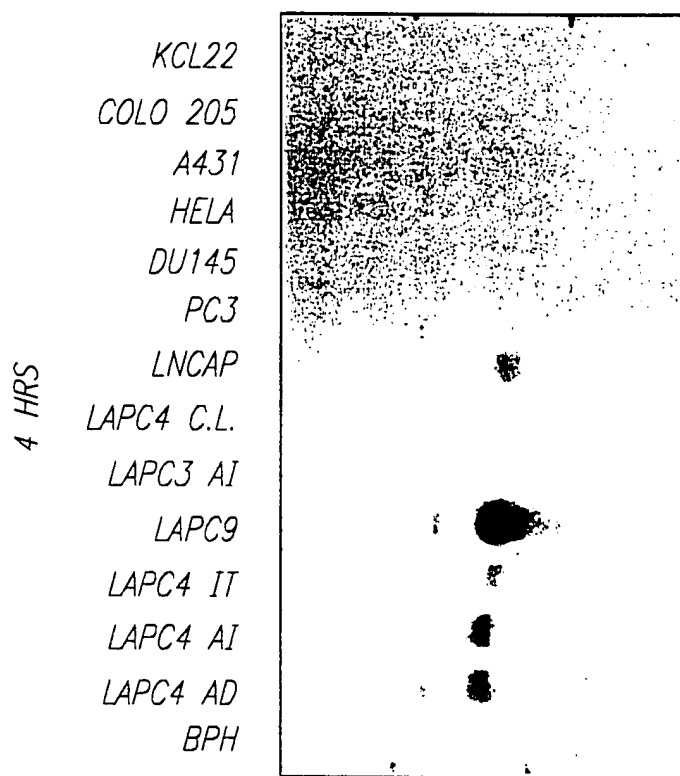
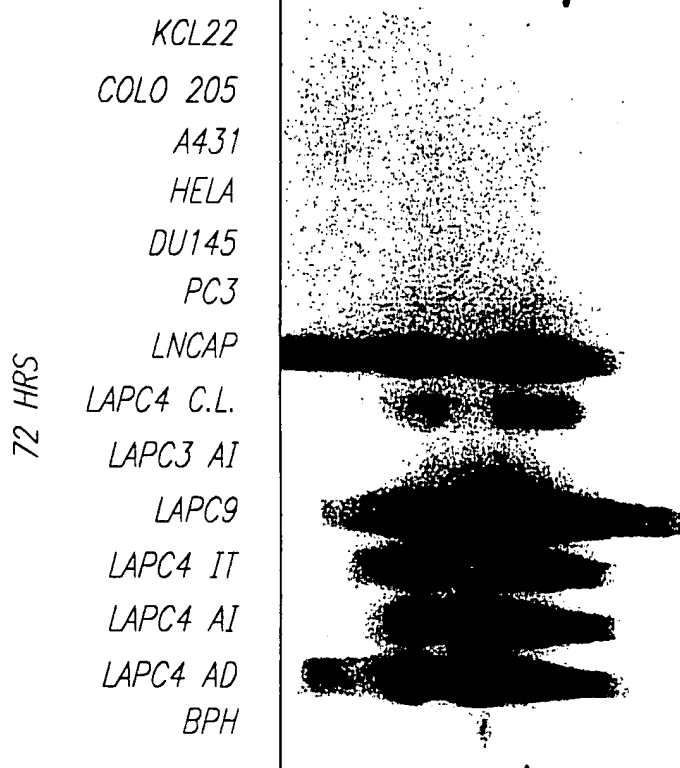
660260 3366560



PSCA

FIG. 10-1

66020" 32E69E60



PSM

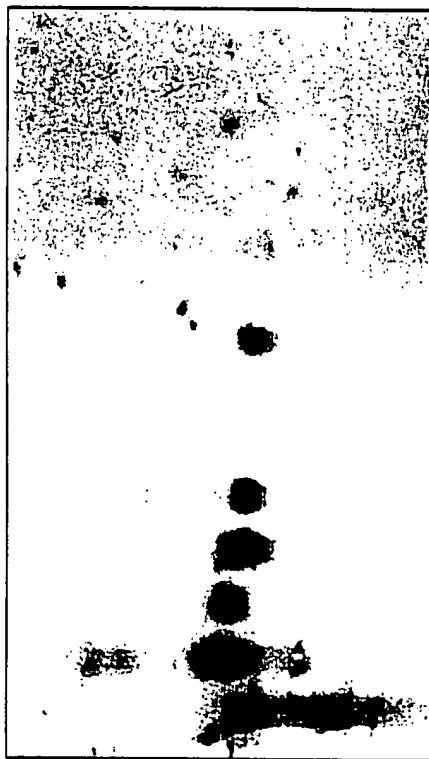
FIG. 10-2

66020" 336560

4 HRS

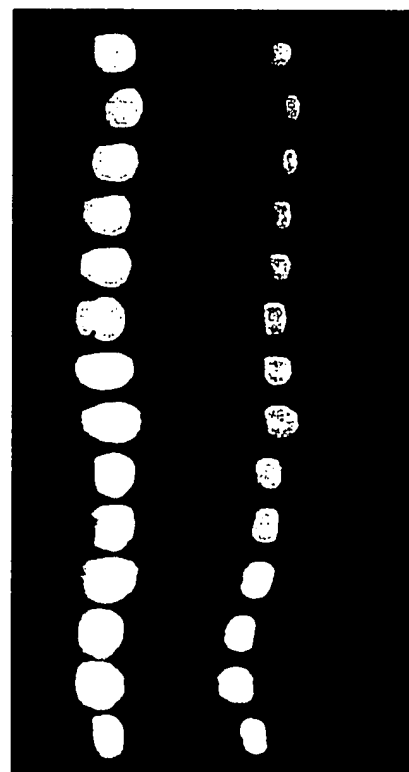
KCL22  
COLO 205  
A431  
HELA  
DU145  
PC3  
LNCAP  
LAPC4 C.L.  
LAPC3 AI  
LAPC9  
LAPC4 IT  
LAPC4 AI  
LAPC4 AD  
BPH

PSA



72 HRS

KCL22  
COLO 205  
A431  
HELA  
DU145  
PC3  
LNCAP  
LAPC4 C.L.  
LAPC3 AI  
LAPC9  
LAPC4 IT  
LAPC4 AI  
LAPC4 AD  
BPH



ETBR

FIG. 10-3

FIG. 11A



FIG. 11B

500220" 9265660

60020" 9269260

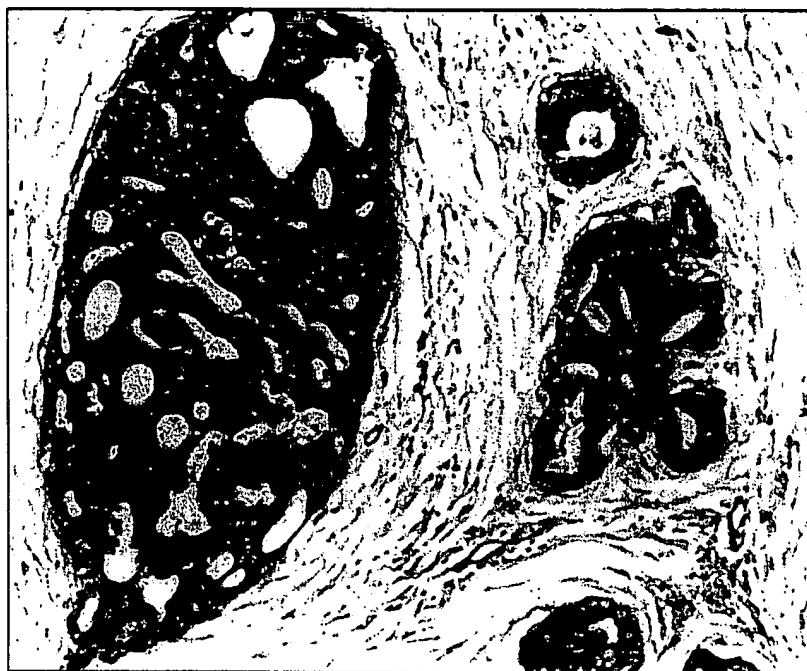


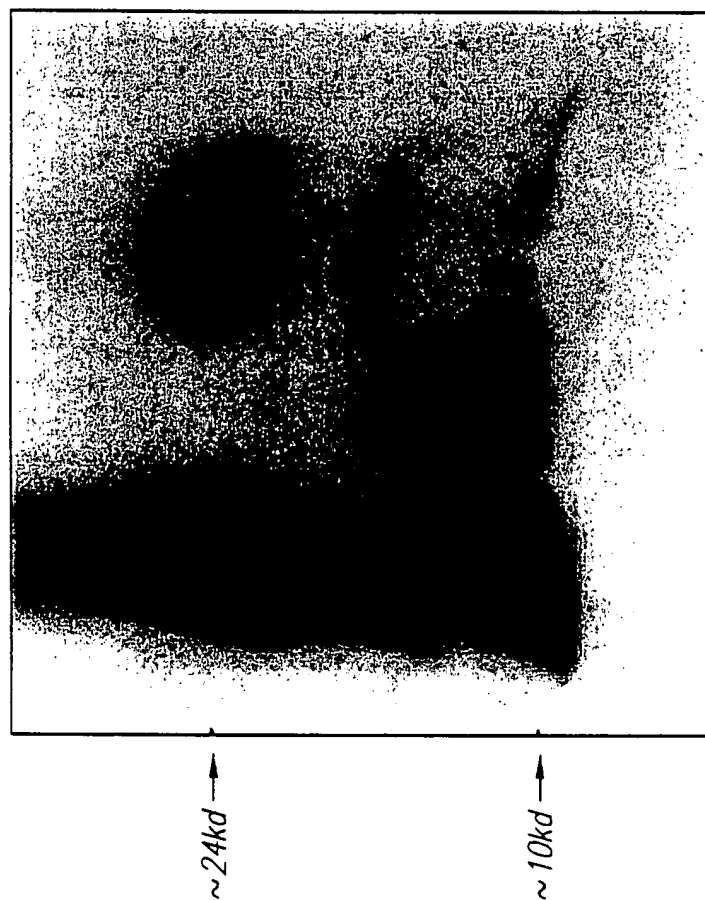
FIG. 11C



660620" 32263260

FIG. 12A

CONTROL  
N GLYCOSIDASE F  
O GLYCOSIDASE



CELL ASSOCIATED

SECRETED

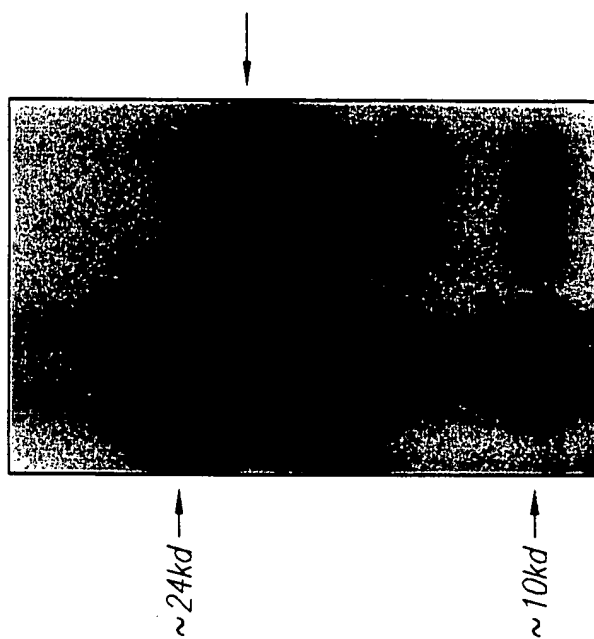


FIG. 12B

66020" 306560

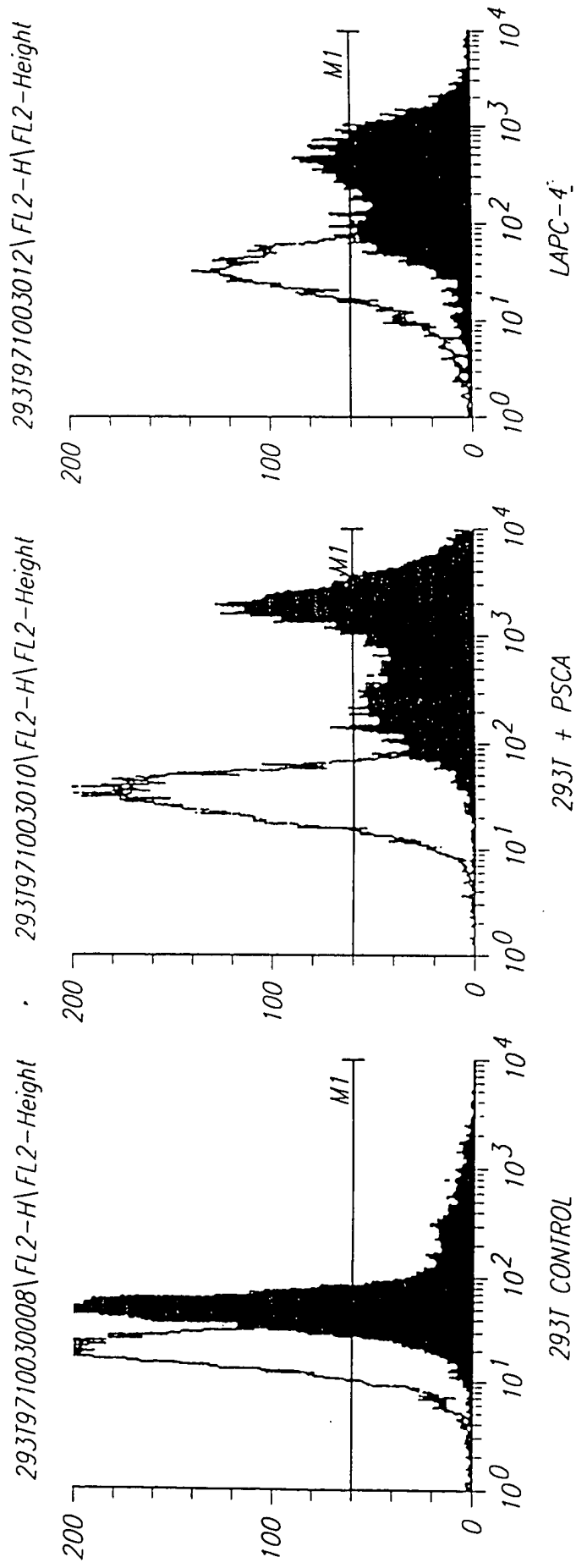
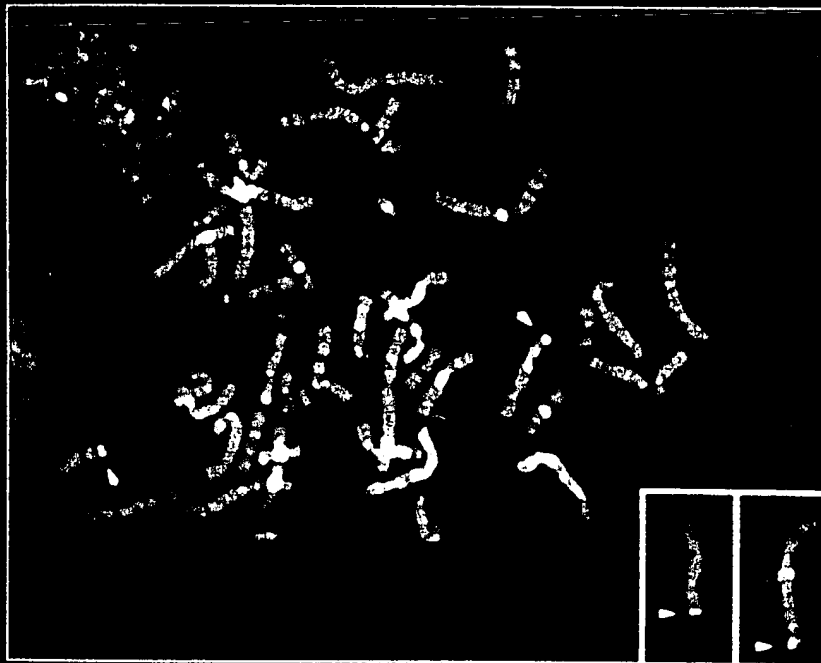


FIGURE 12C

## PSCA Maps to Chromosome 8q24.2



Fluorescent  
in Situ Hybridization  
Analysis of PSCA

FIGURE 13

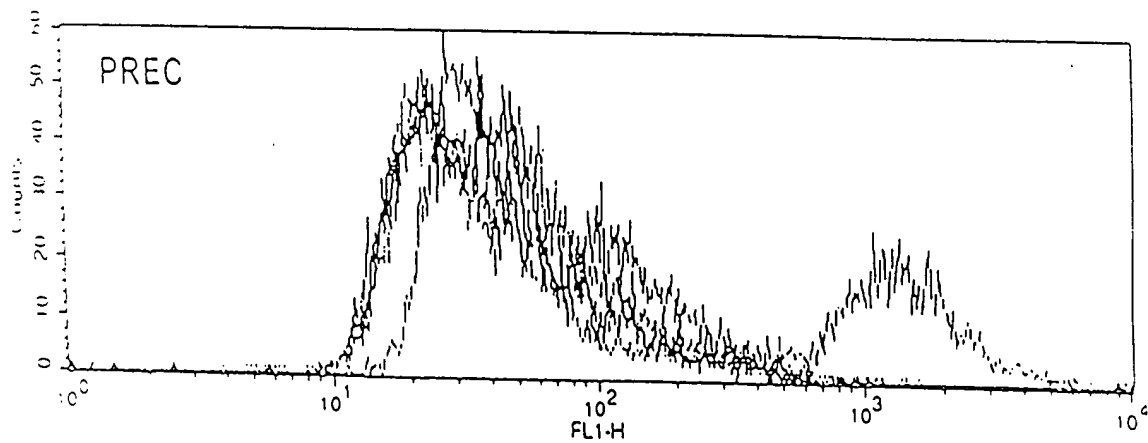
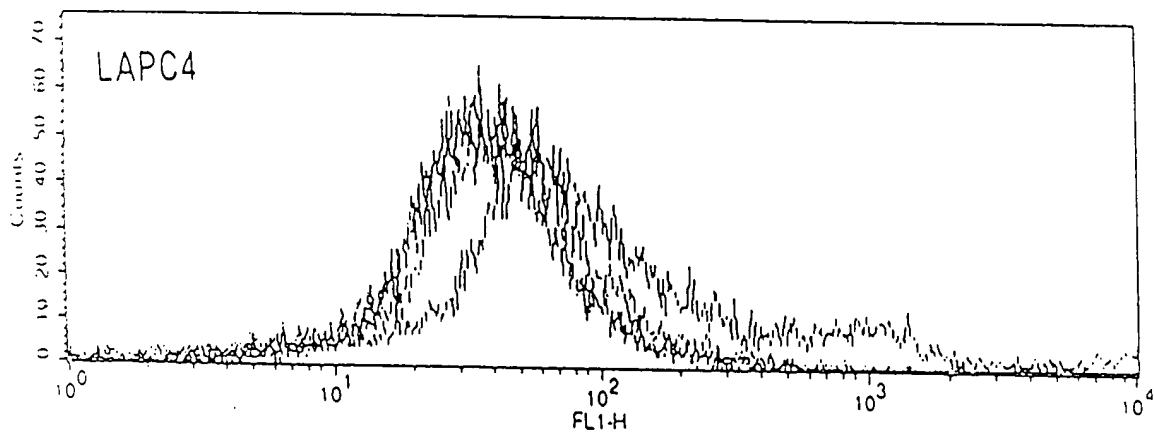
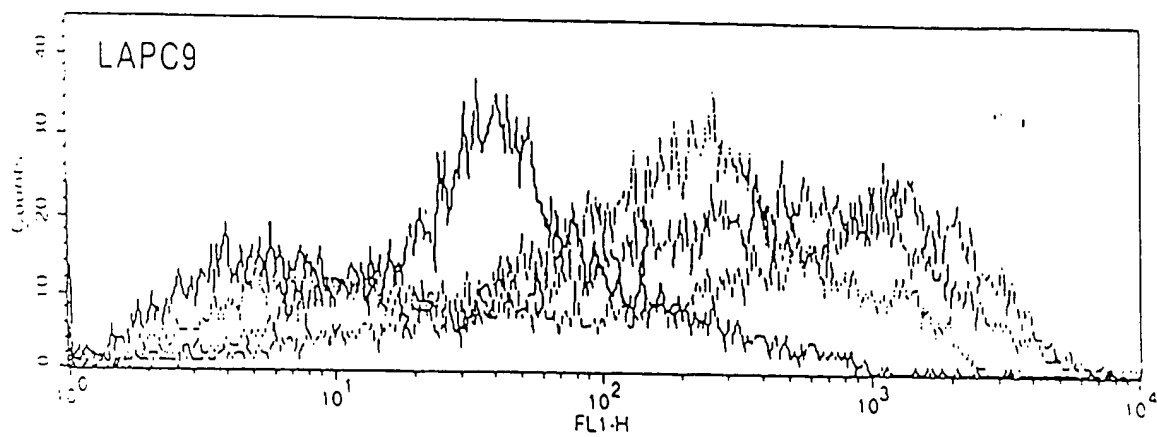


FIGURE 14

**A**

		Epitope map			
mAb	Isotype	FL (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1 k	2.039	0.007	0.628	0.000
2H9	IgG1 k	1.318	0.863	0.032	0.021
3C5	IgG2a k	2.893	1.965	0.016	0.005
3E6	IgG3 k	0.328	0.024	0.069	0.370
4A10	IgG2a k	2.039	1.315	0.000	0.014
2A2	IgG2a k	1.366	0.733	0.010	0.003
3G3	IgG2a k	2.805	1.731	0.004	0.000

**B**

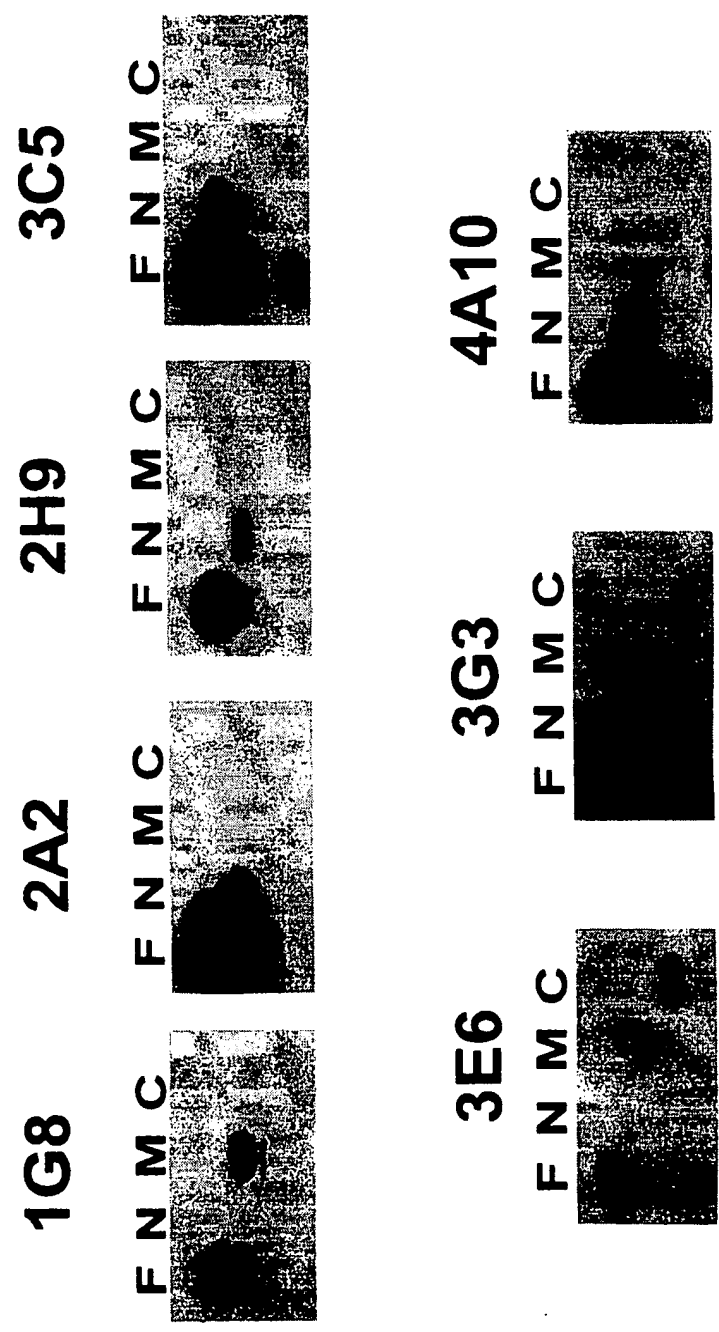


FIGURE 15

# Prostate Stem Cell Antigen (PSCA) is a GPI-anchored Protein

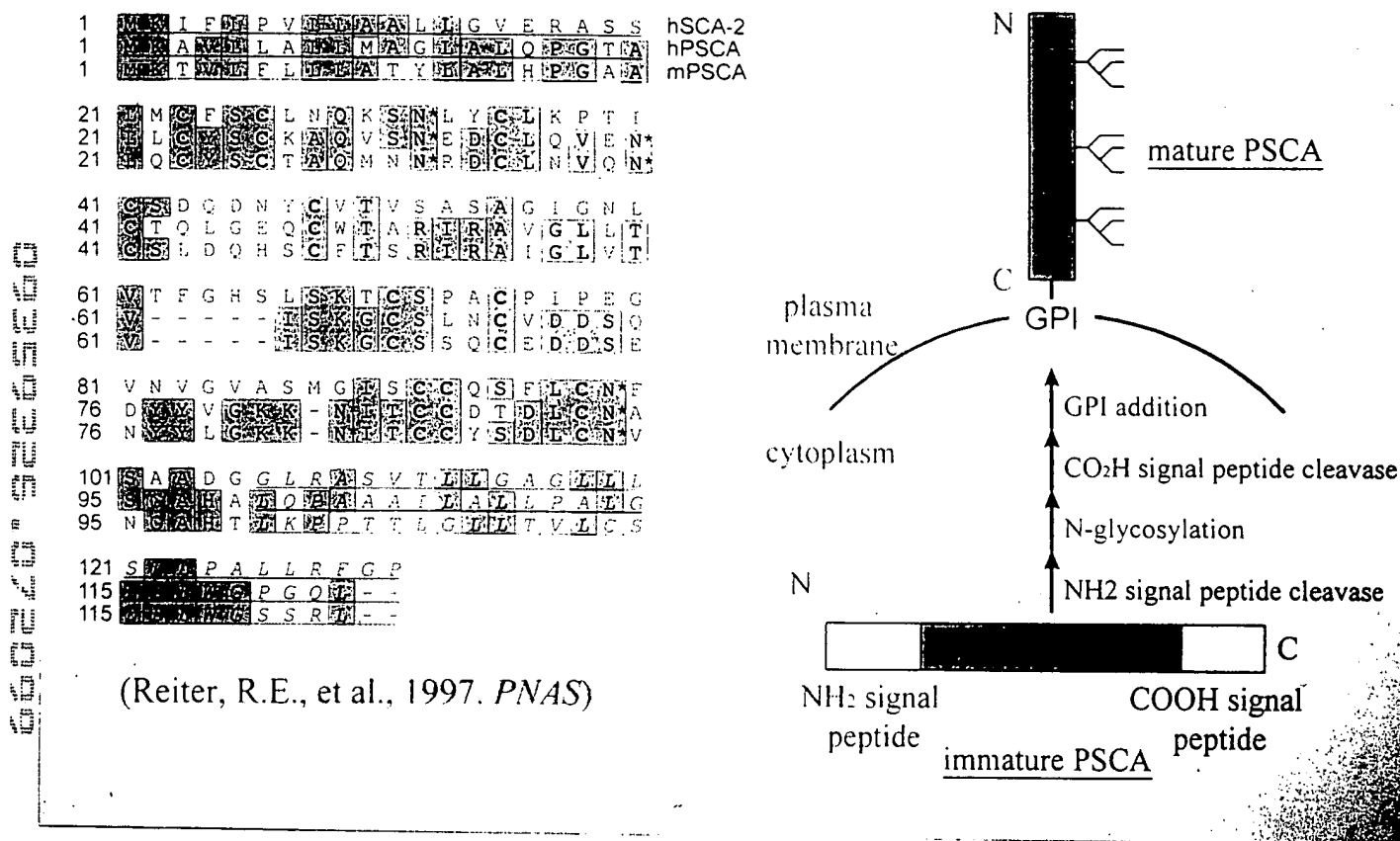
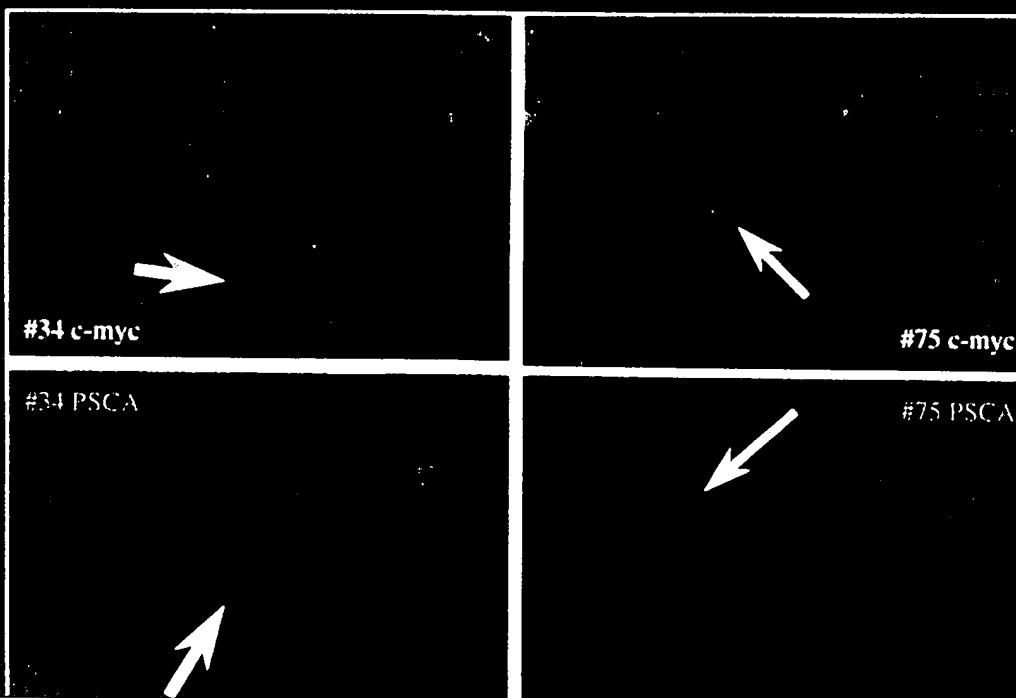


FIGURE 16

# FISH Analysis of PSCA and c-myc in Prostate Cancer

Gain Chromosome 8

Amplification



*R. Jenkins*

FIGURE 17

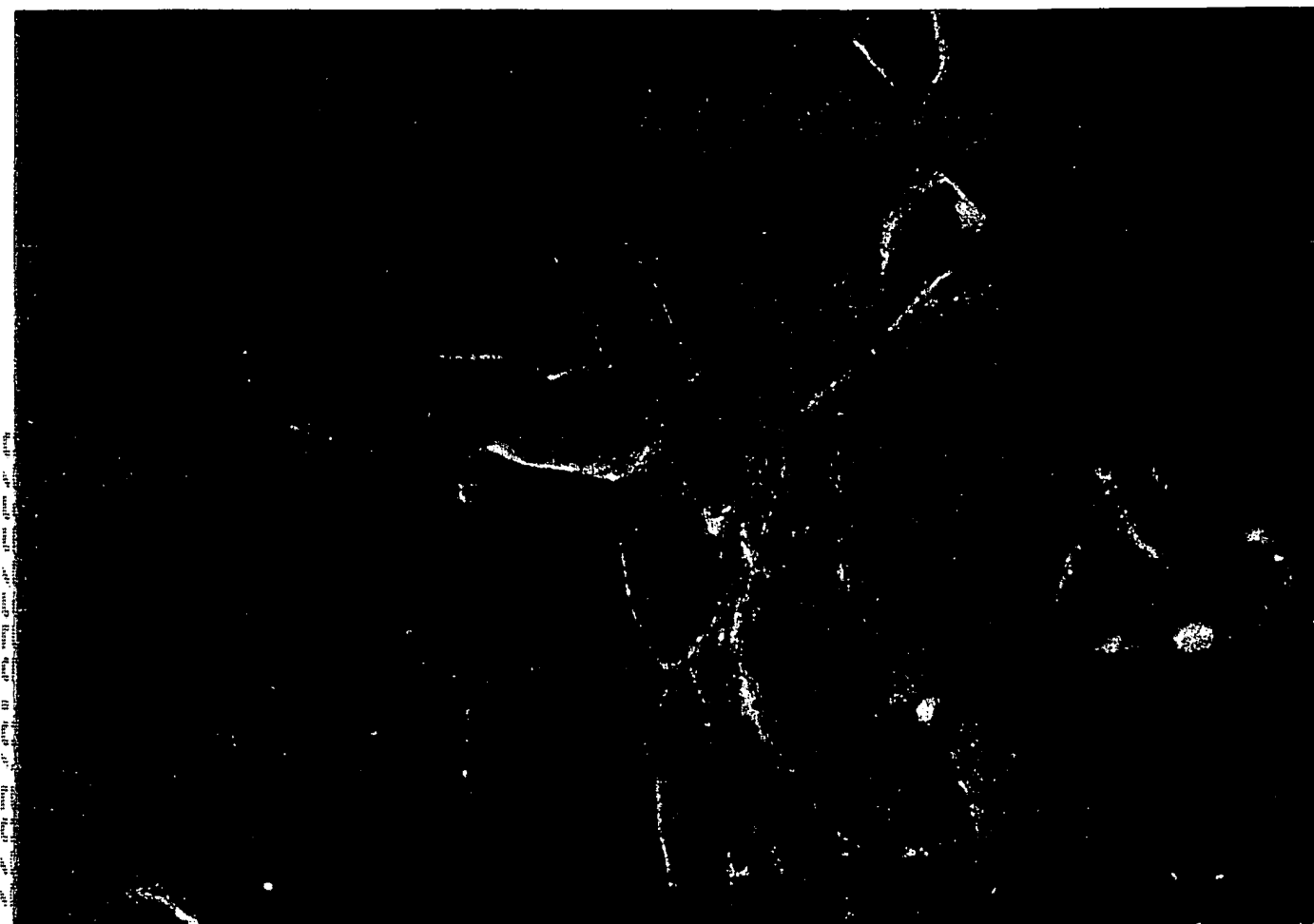


FIGURE 18



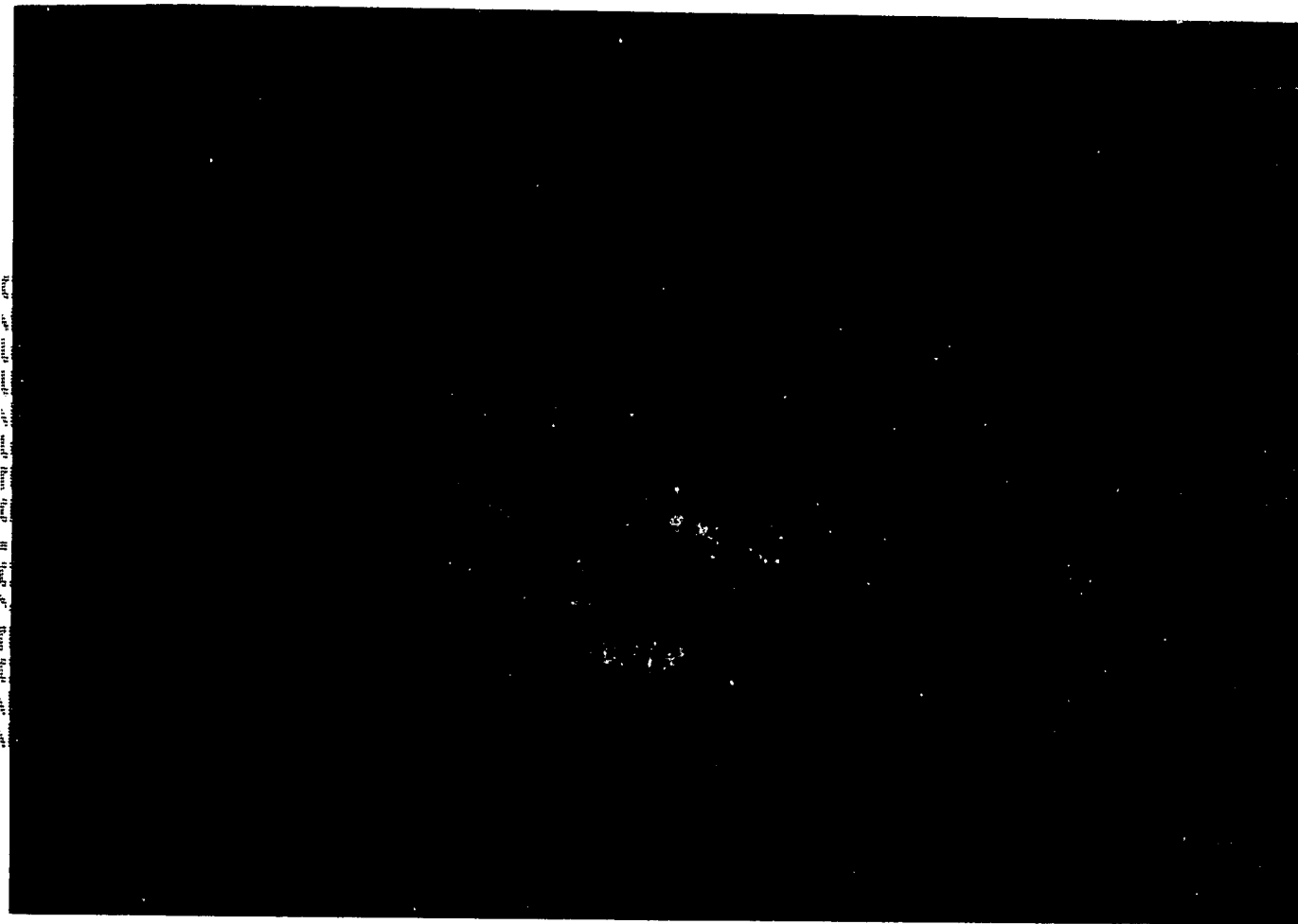


FIGURE 19

150020" 92E05E00



FIGURE 20

## PSCA Immunostaining of Primary Tumors

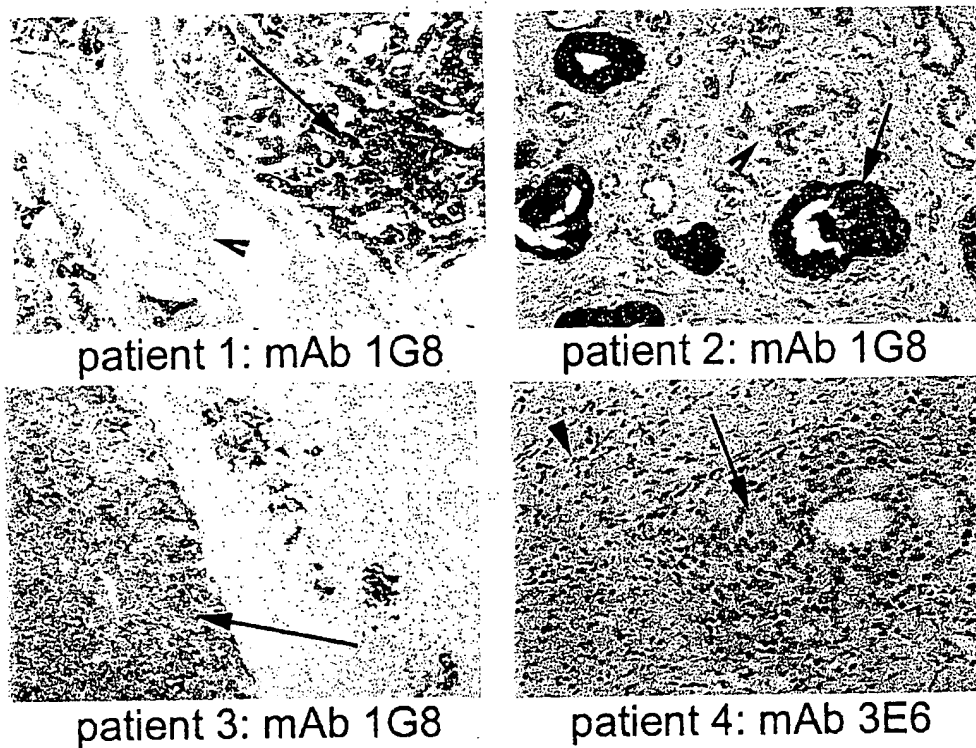


FIGURE 21



FIGURE 22

660220 926560

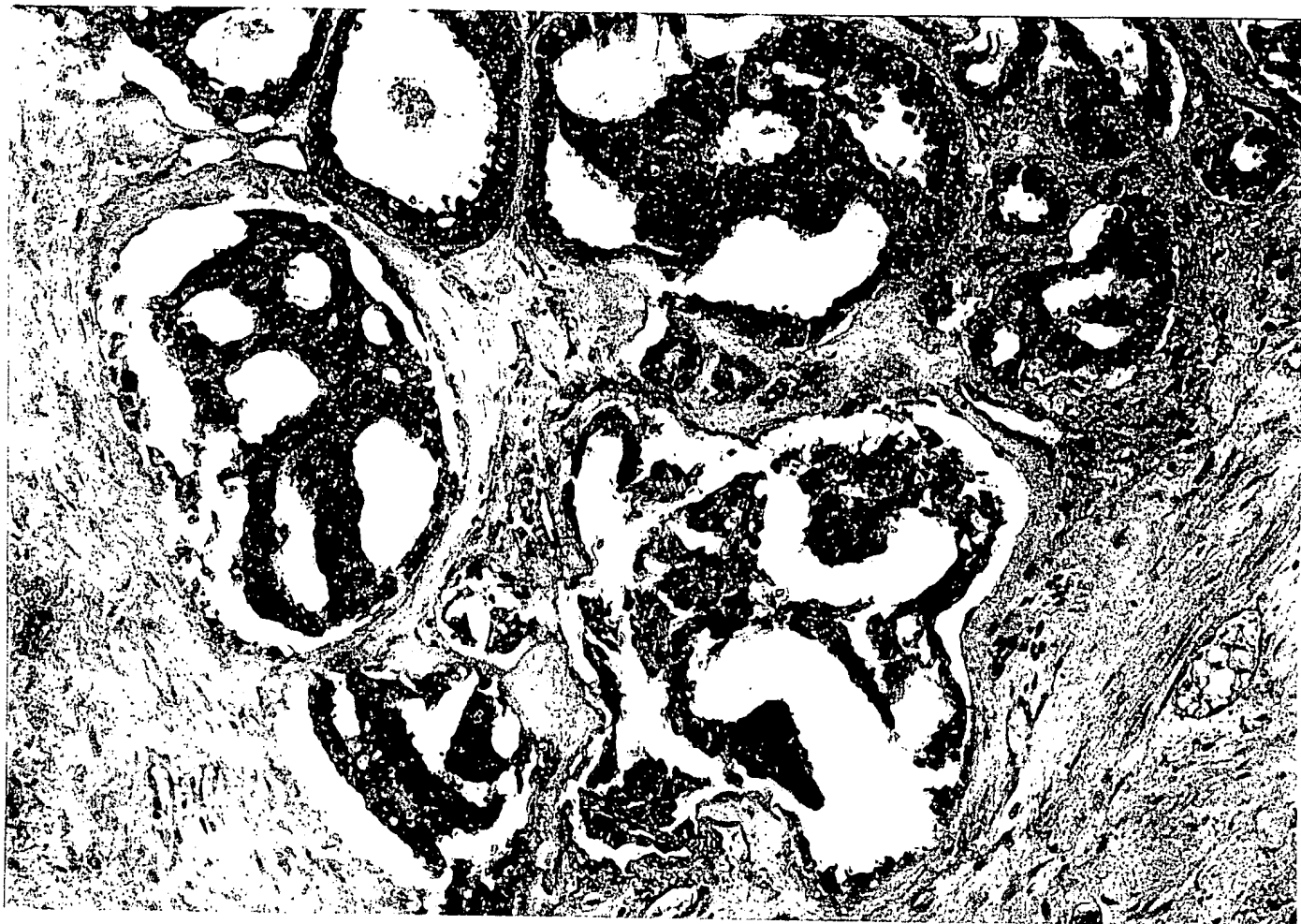


FIGURE 23

660240 92265260

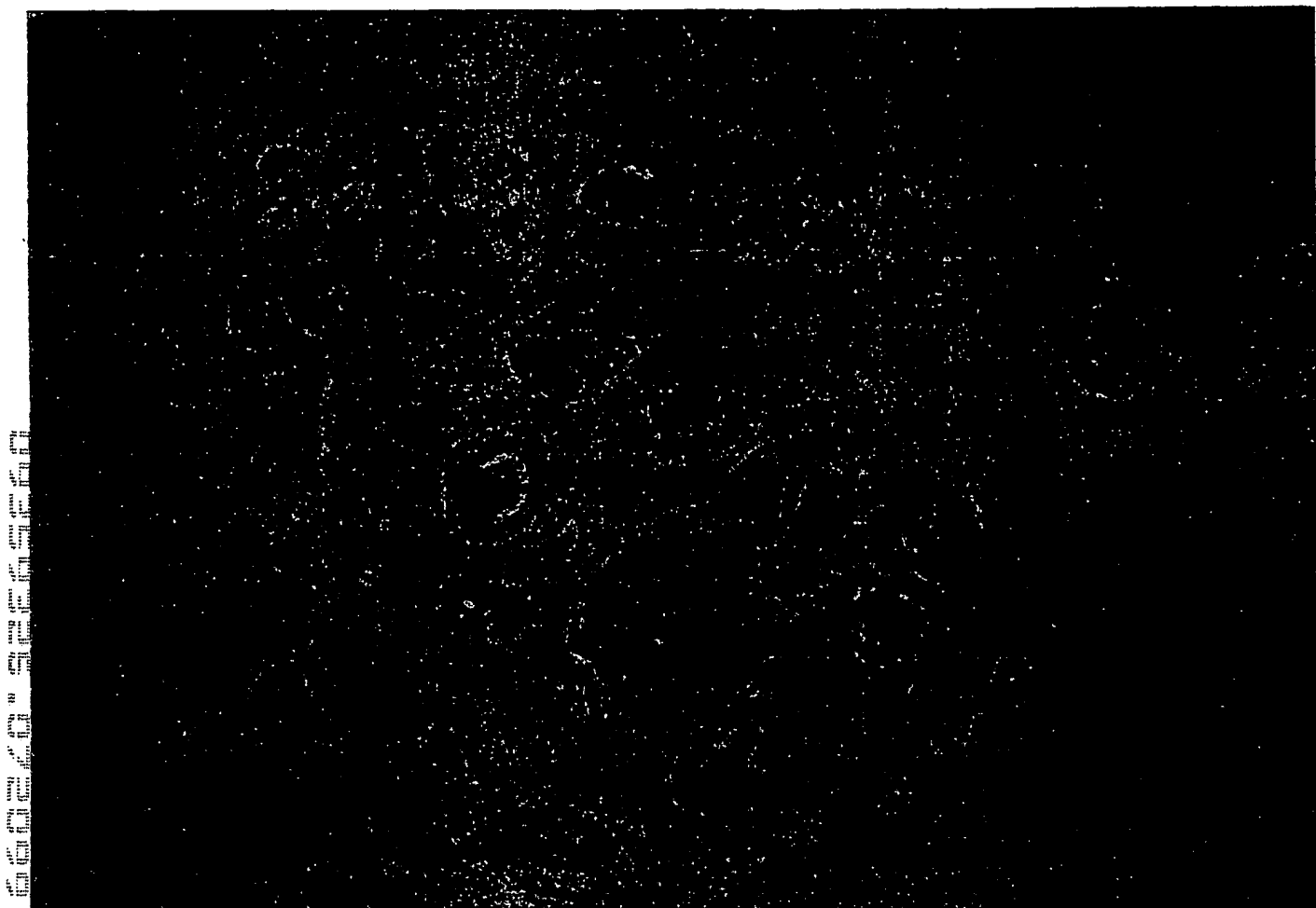


**FIGURE 24**

No. 1008 & PSCA  
Circuit / 4 hr exp

Noted & PSCA  
2/28/44 exp

FIGURE 25



**FIGURE 26**



66020 3263260

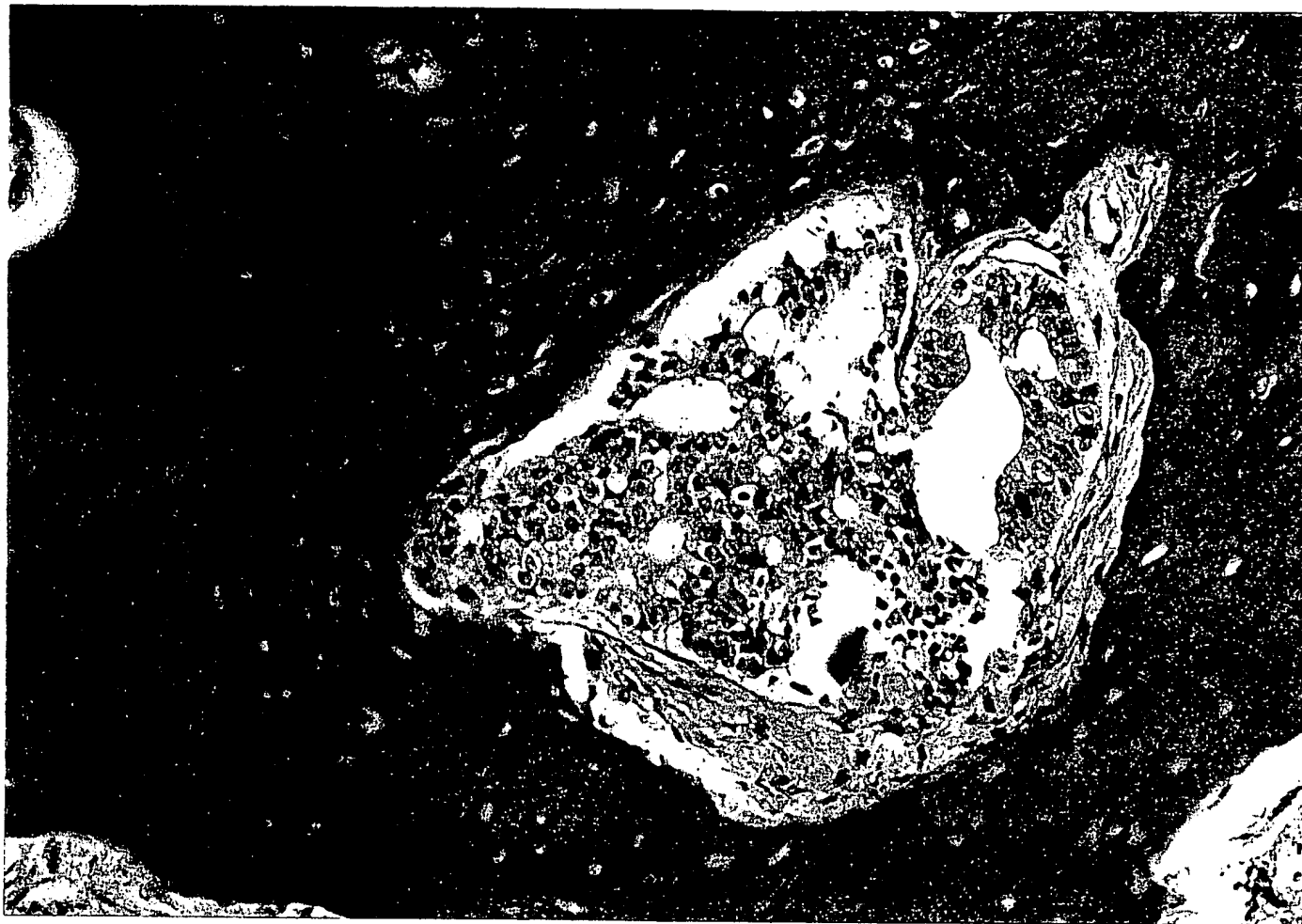
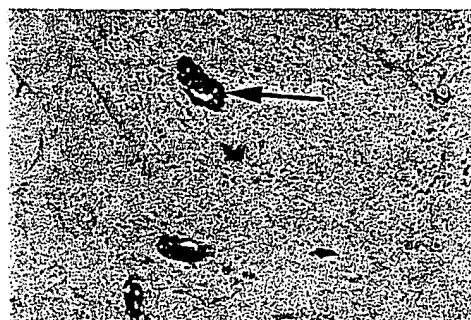
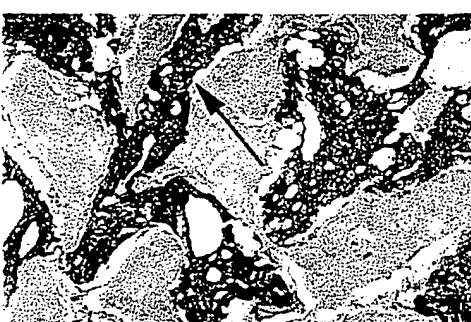


FIGURE 27

## PSCA Immunostaining of Bony Metastases



Patient 5: H and E  
and mAb 1G8



Patient 4: H and E  
and mAb 3E6

FIGURE 28

66020' 926560

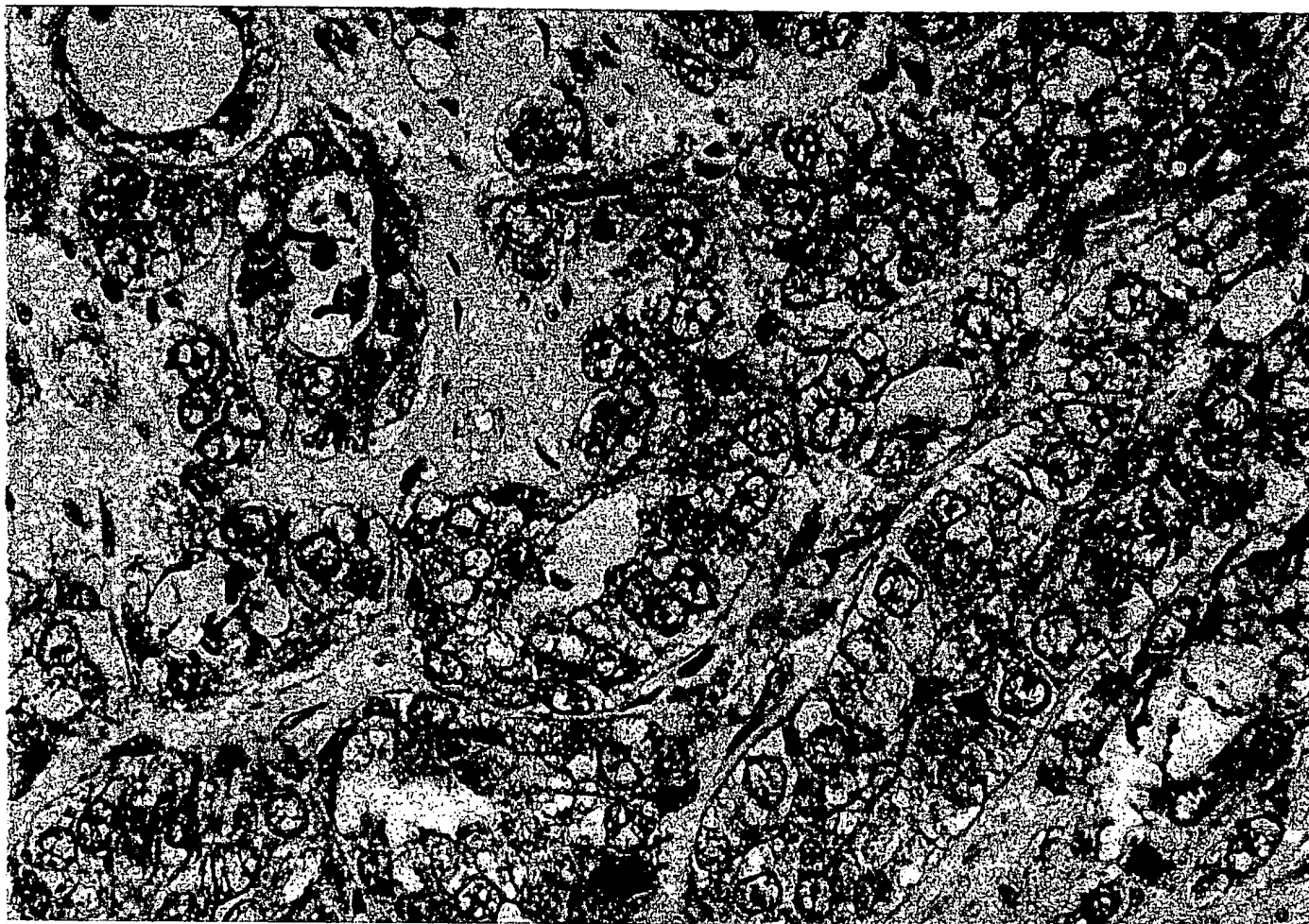
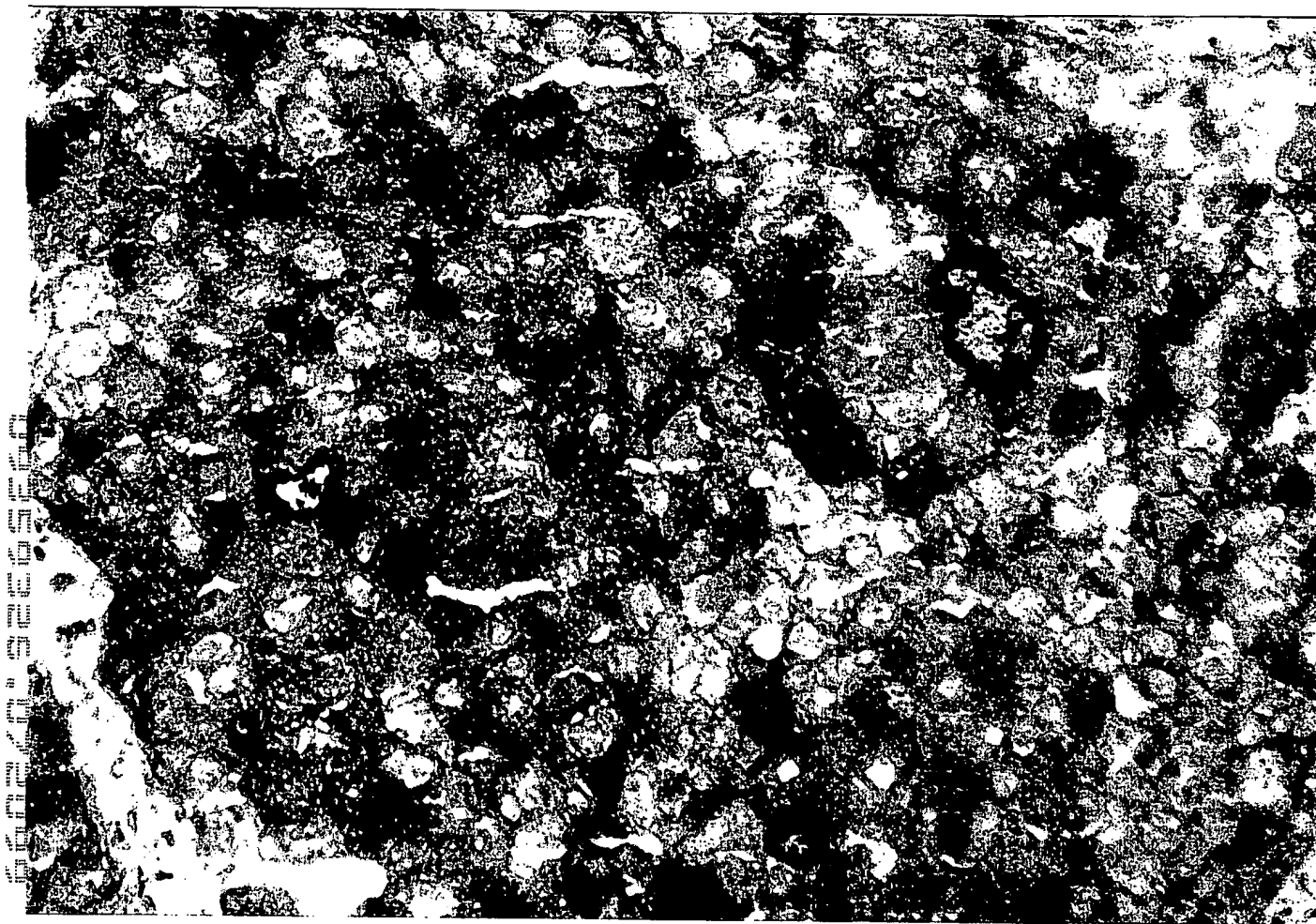


FIGURE 29



**FIGURE 30**

660320" 92655260

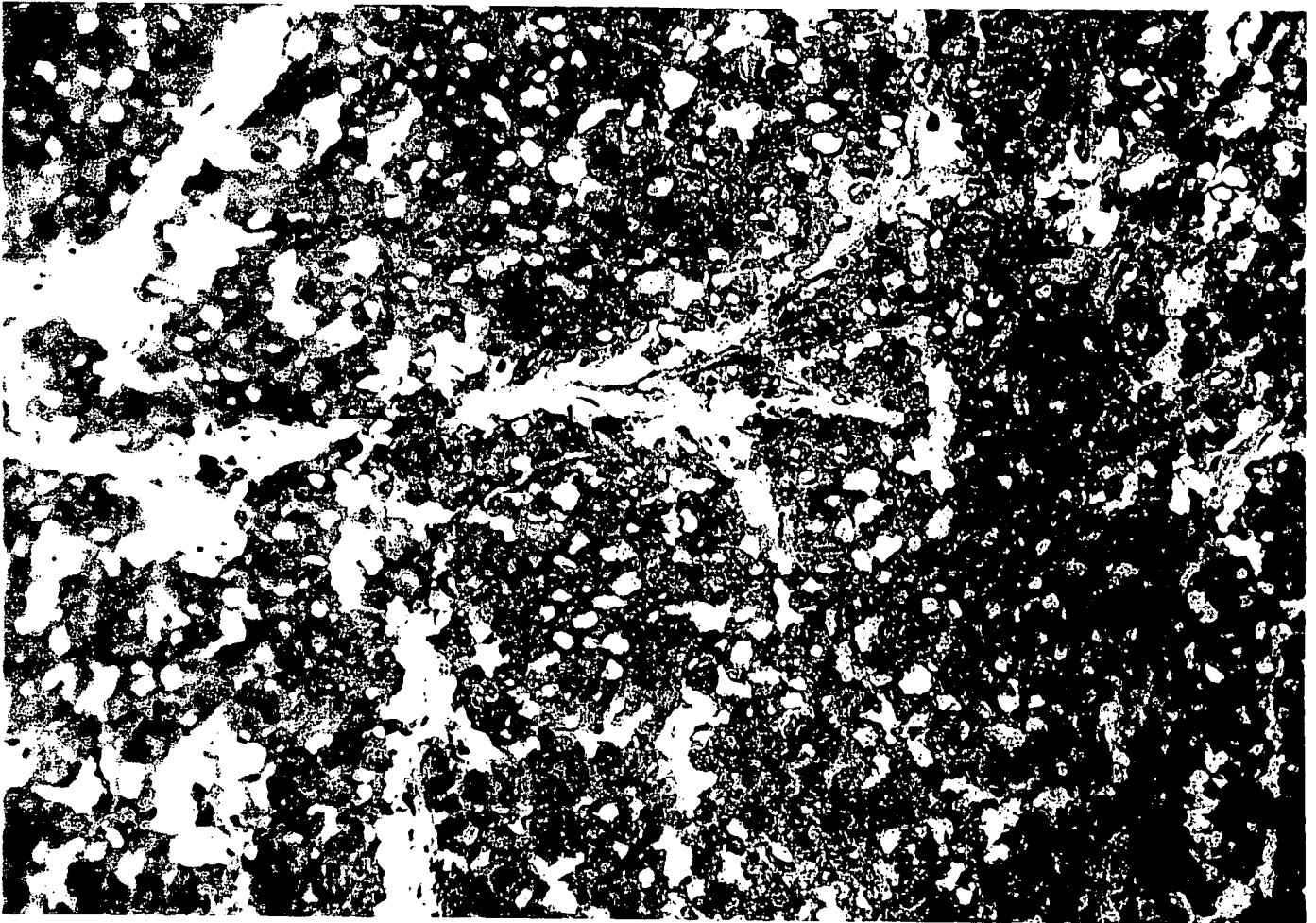


FIGURE 31

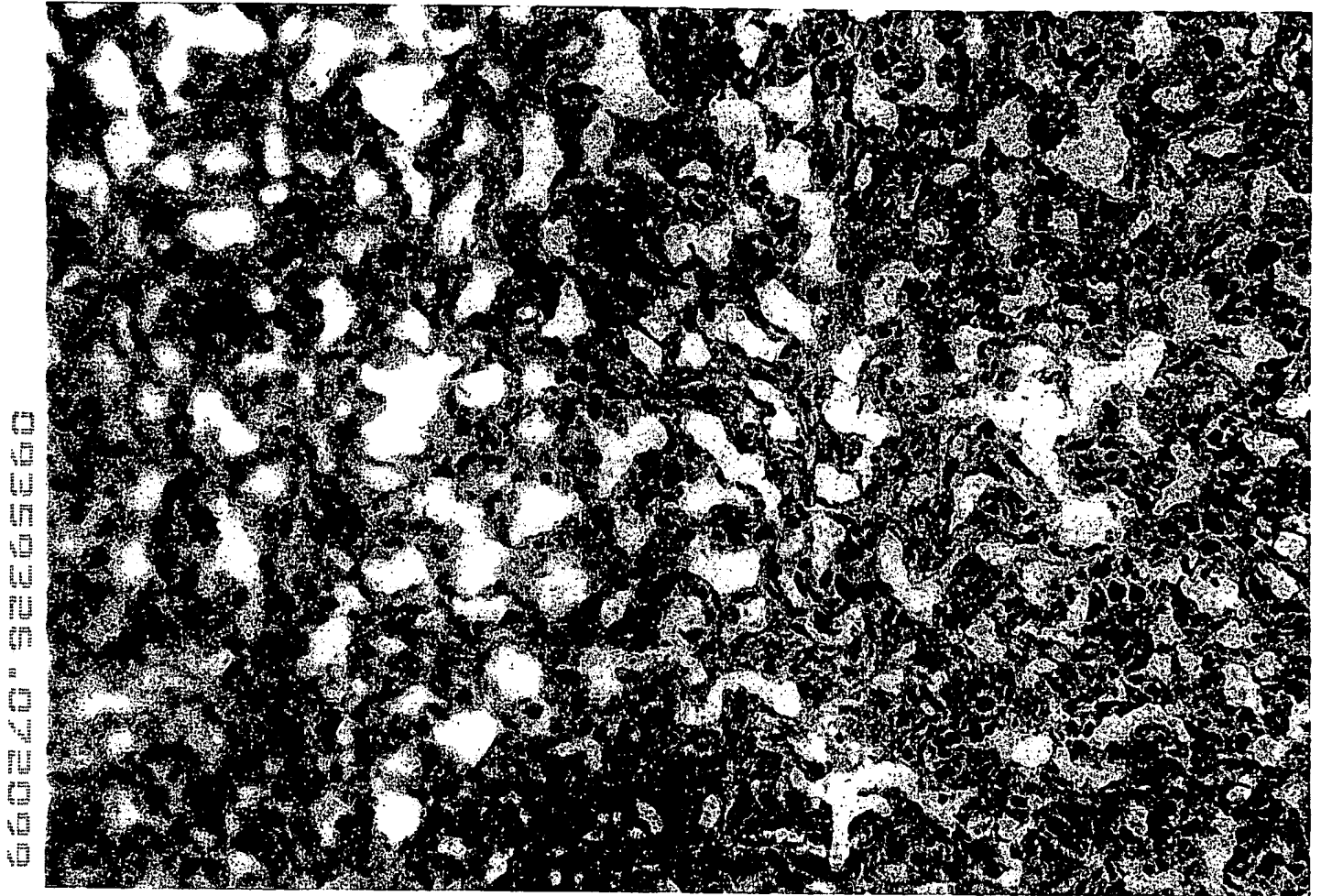


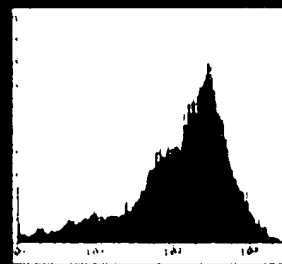
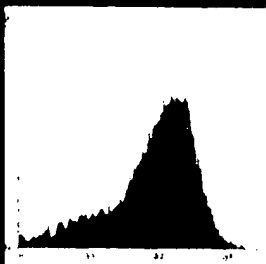
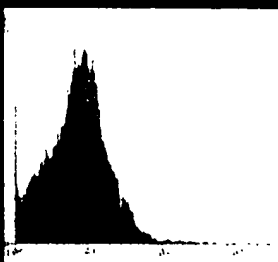
FIGURE 32

# PSCA Expression in LAPC-9 Xenograft by FACS

Secondary Antibody

1G8

2H9



4A10

3C5

3E6

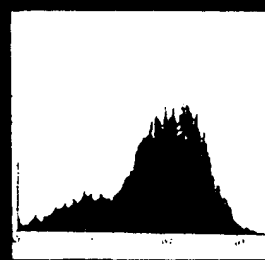
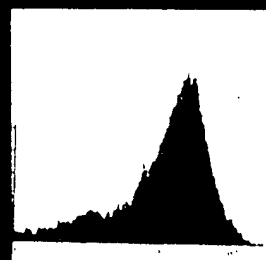
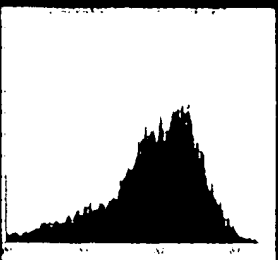


FIGURE 33

60020 336560

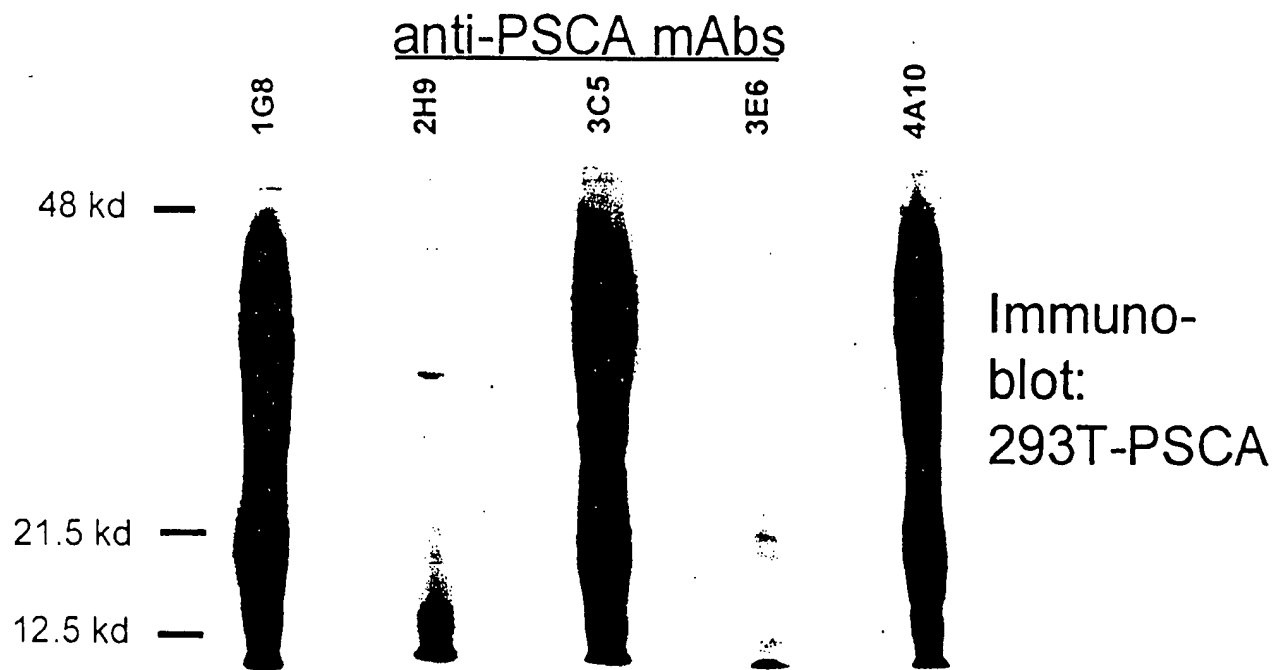


FIGURE 34



## Immunofluorescent Staining of LNCaP-PSCA Cells

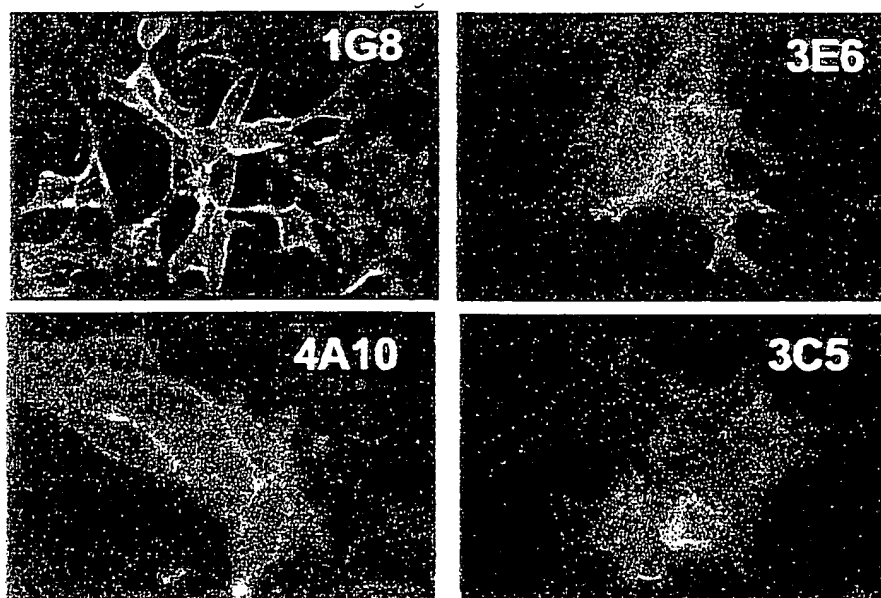


FIGURE 35

[illegible]

FIGURE 36

66020" 32265200

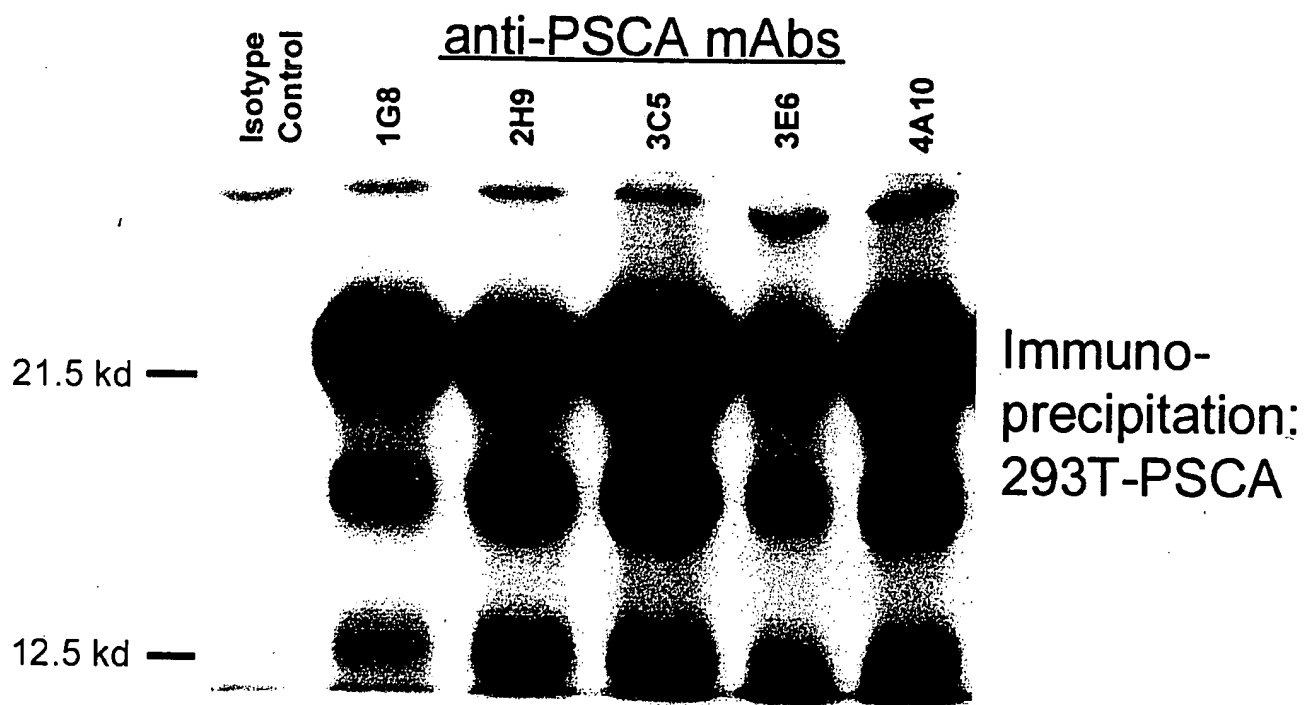
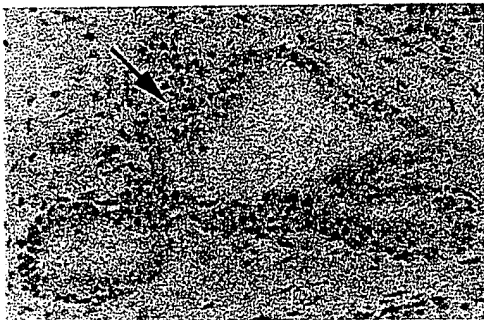


FIGURE 37

## Immunohistochemical Staining of Normal Prostate

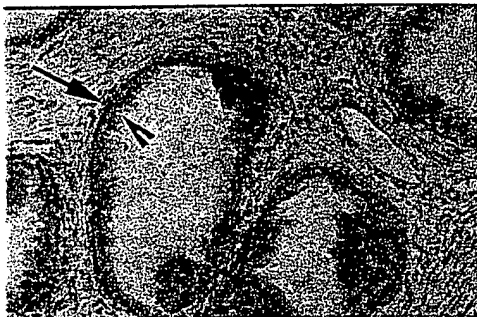
Normal: Isotype Control



Normal: PSCA mAb 3E6



Normal: PSCA mAb 1G8



Atrophy: PSCA mAb 2H9

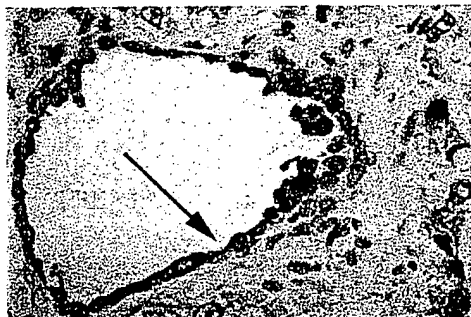


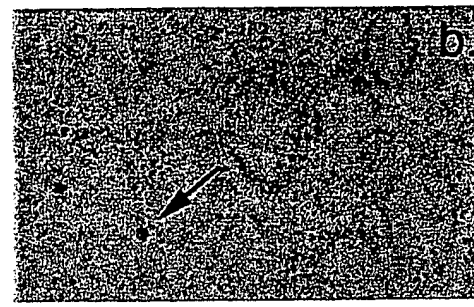
FIGURE 38

660220" 92E69E60

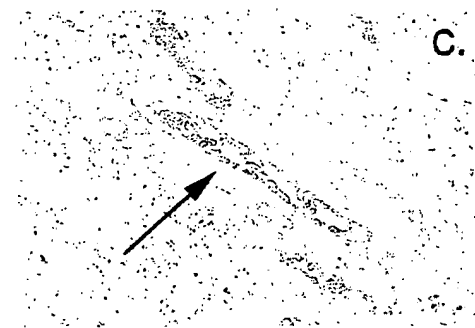
A.



Bladder: 1G8



Colon: 1G8



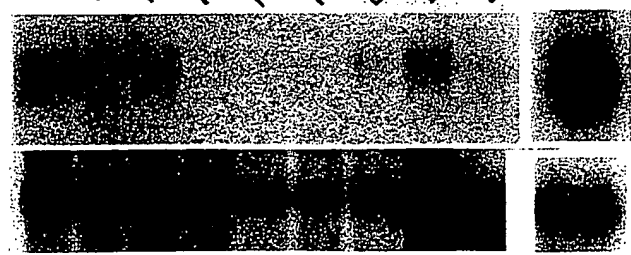
Kidney: 3E6



Placenta: 3E6

B.

Prostate  
Prostate  
Prostate  
Kidney  
Kidney  
Kidney  
Bladder  
Bladder  
Bladder  
LAPC 9

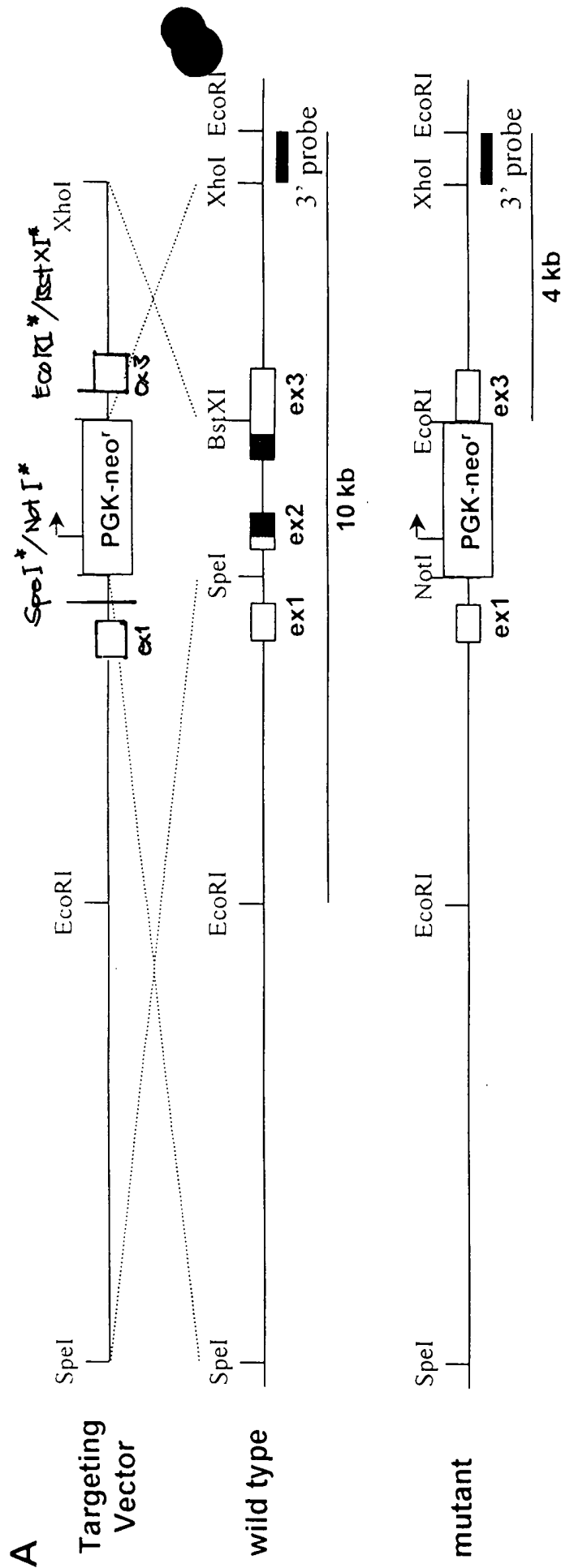


PSCA

Actin

FIGURE 39

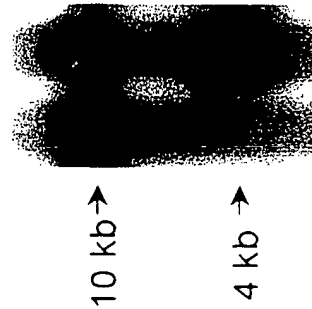
# Targeting of Mouse PSCA Gene



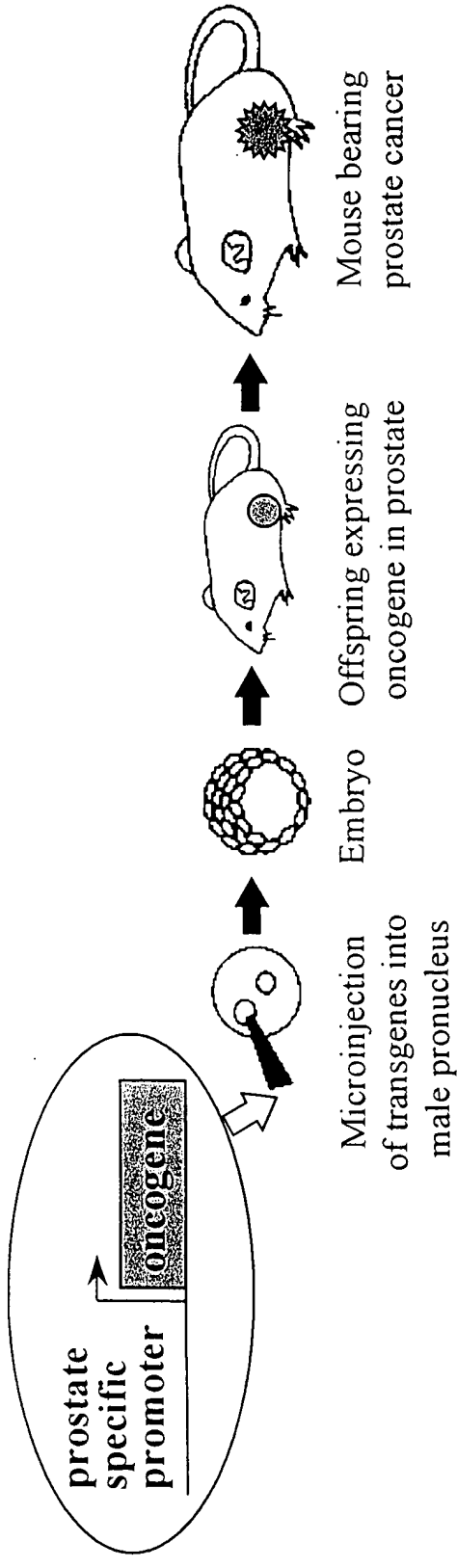
## B. Genomic Southern Analysis of ES Cells

- \* ex1, 2, and 3 are the exons of PSCA gene.
- \* Black boxes of ex2 and ex3 encode PSCA mature protein sequences.
- \* ES genomic DNAs were digested with EcoRI, followed by Southern hybridization using 3' probe.

+/- +/-



# Transgenic Mouse Models of Prostate Cancer



Transgene	Target tissues	Characteristics
C3(1) (-3 kb)/ SV40 large+small, T <i>Maroulakou et al.</i> 1994 <i>PNAS</i>	prostate (secretory cells) urethral, mammary and sweat gland	Low-grade PIN 8-12 wks High-grade PIN 8-12 wks Invasive carcinoma 28 wks No metastases
Probasin (-426 bp)/ SV40 large+small, T <i>Greenberg et al.</i> 1995 <i>PNAS</i>	prostate (secretory cells)	Low-grade PIN 5-8 wks High-grade PIN 8-12 wks Invasive carcinoma 12 wks Metastases in lymph node, lung, liver and bone
Cryptdin2 (-6.5 kb)/ SV40 large+small, T <i>Garabedian et al.</i> 1998 <i>PNAS</i>	prostate (neuroendocrine cells) small intestine	Low-grade PIN 8-12 wks High-grade PIN 8-12 wks Invasive carcinoma 16 wks Metastases in lymph node, lung, liver and bone

# Reporter Gene Constructs for Transfection Assay

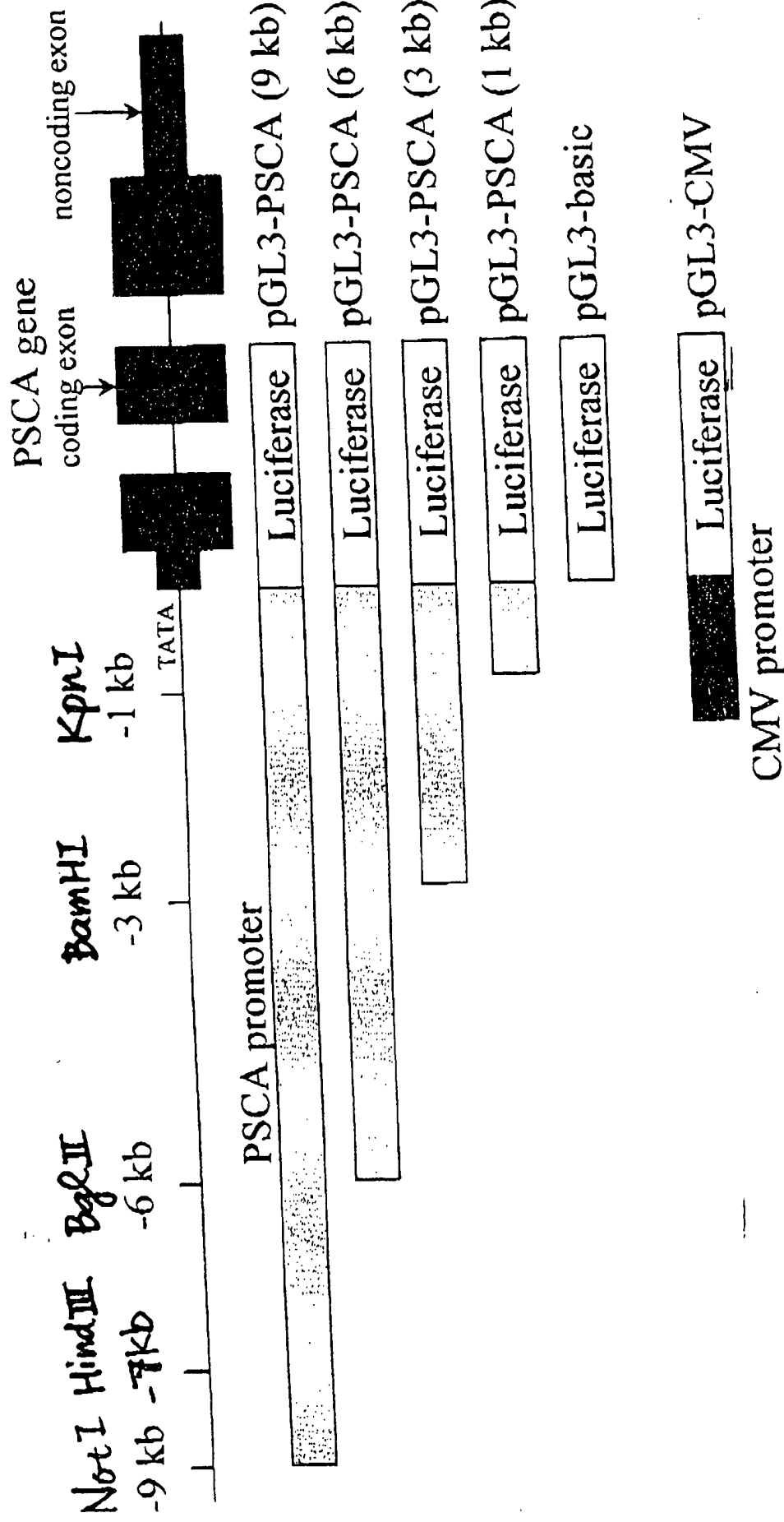


FIGURE 42



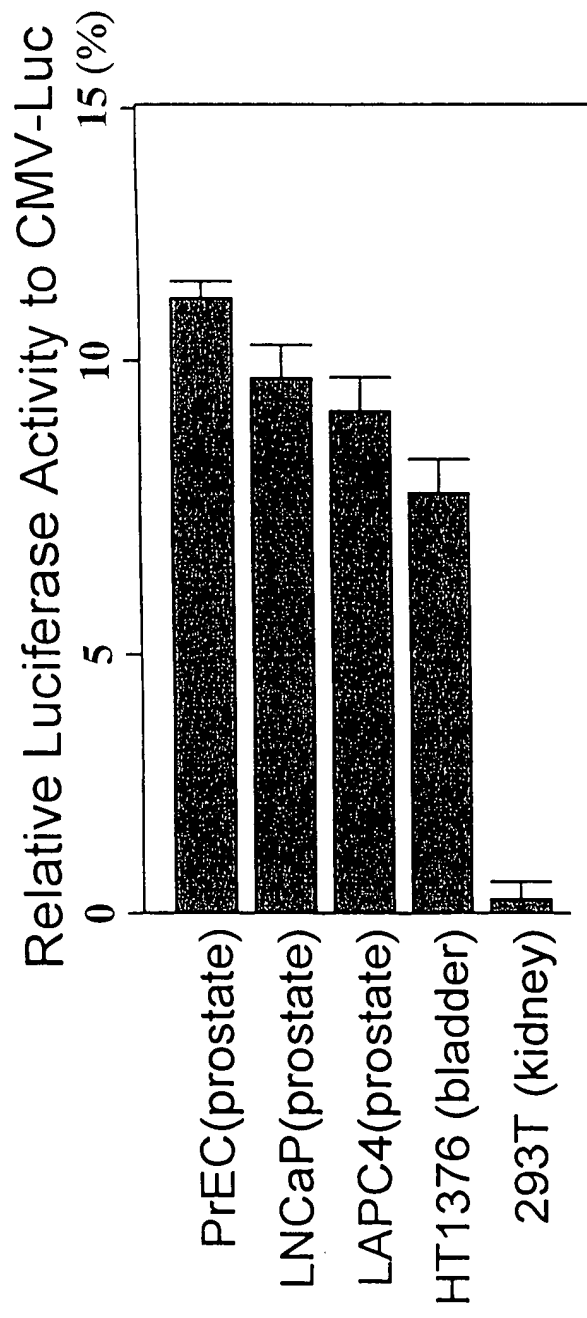


FIGURE 43

# Identification of Prostate-Specific Elements Within PSCA Promoter Sequences

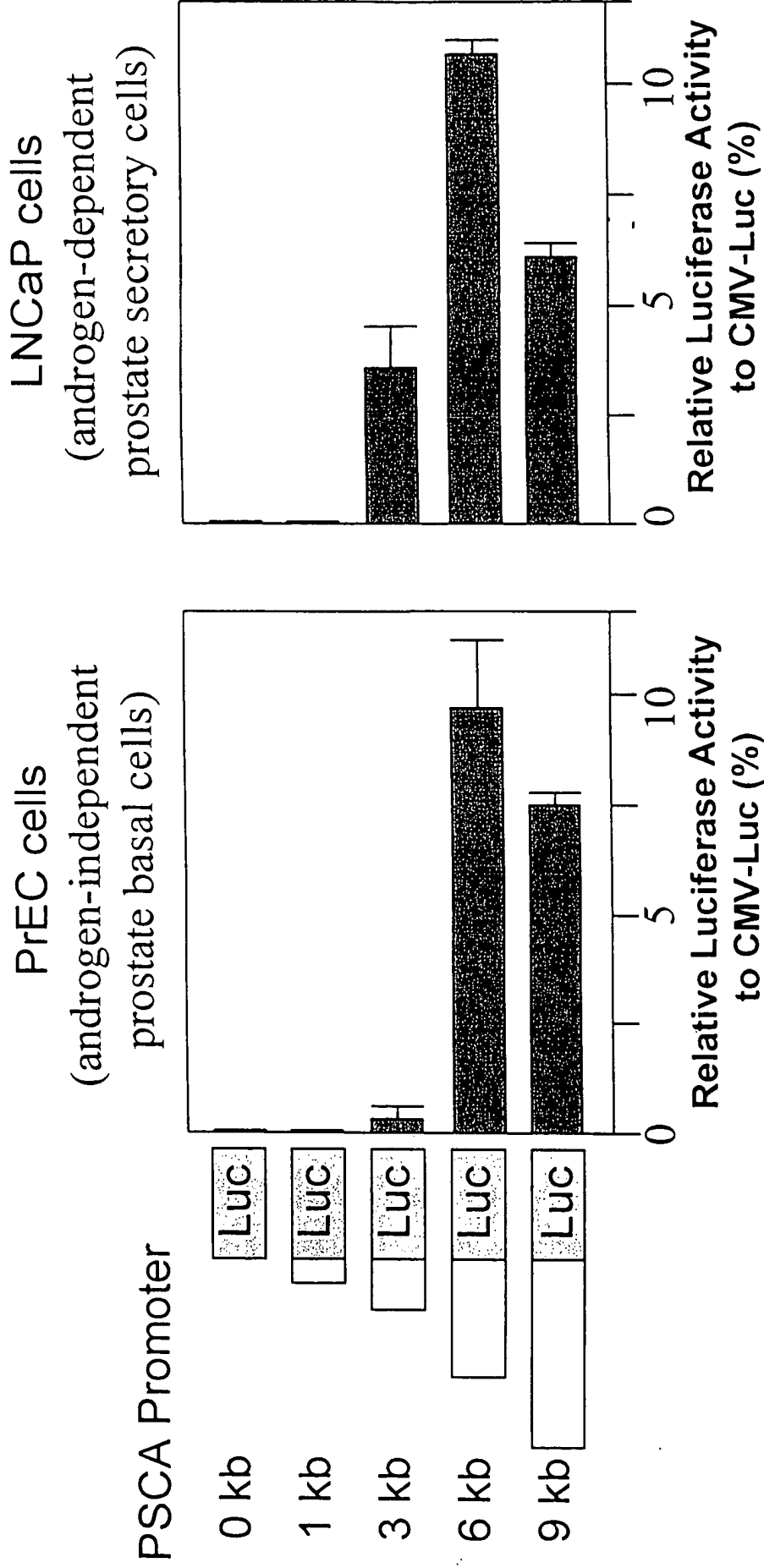


FIGURE 44

# Update of Transgenic Mouse Projects

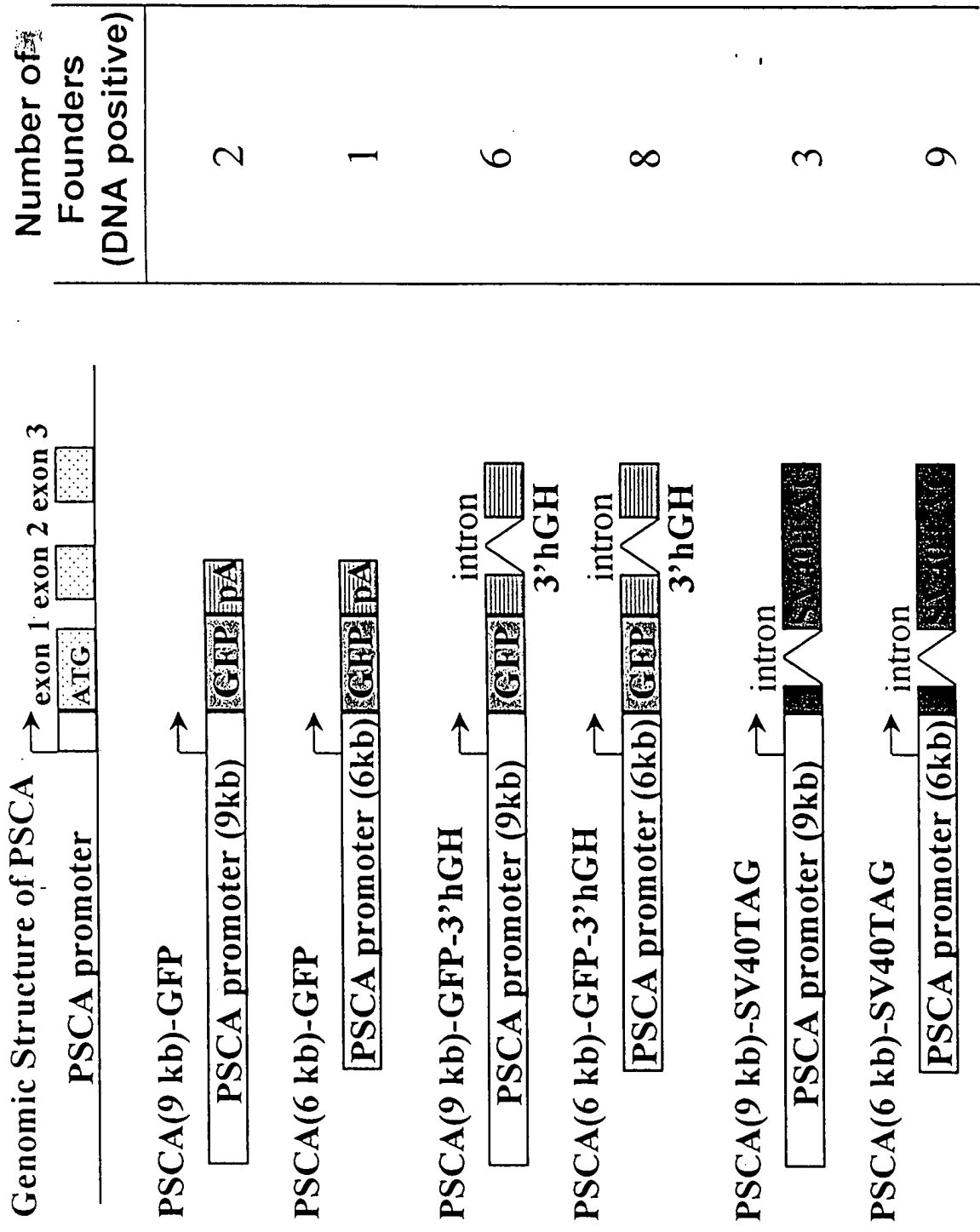


FIGURE 45

Whole-mount green fluorescence image

Negative tissues

- Stomach
- Small intestine
- Colon
- Seminal Vesicle
- Urethra
- Testis
- Liver
- Kidney
- Lung
- Brain
- Heart
- Skeletal muscle
- Ovary
- Uterus

Prostate  
(A25-106-2)

Bladder  
(A25-104)

Skin  
(A25-106-2)

Transgenic

Non-transgenic

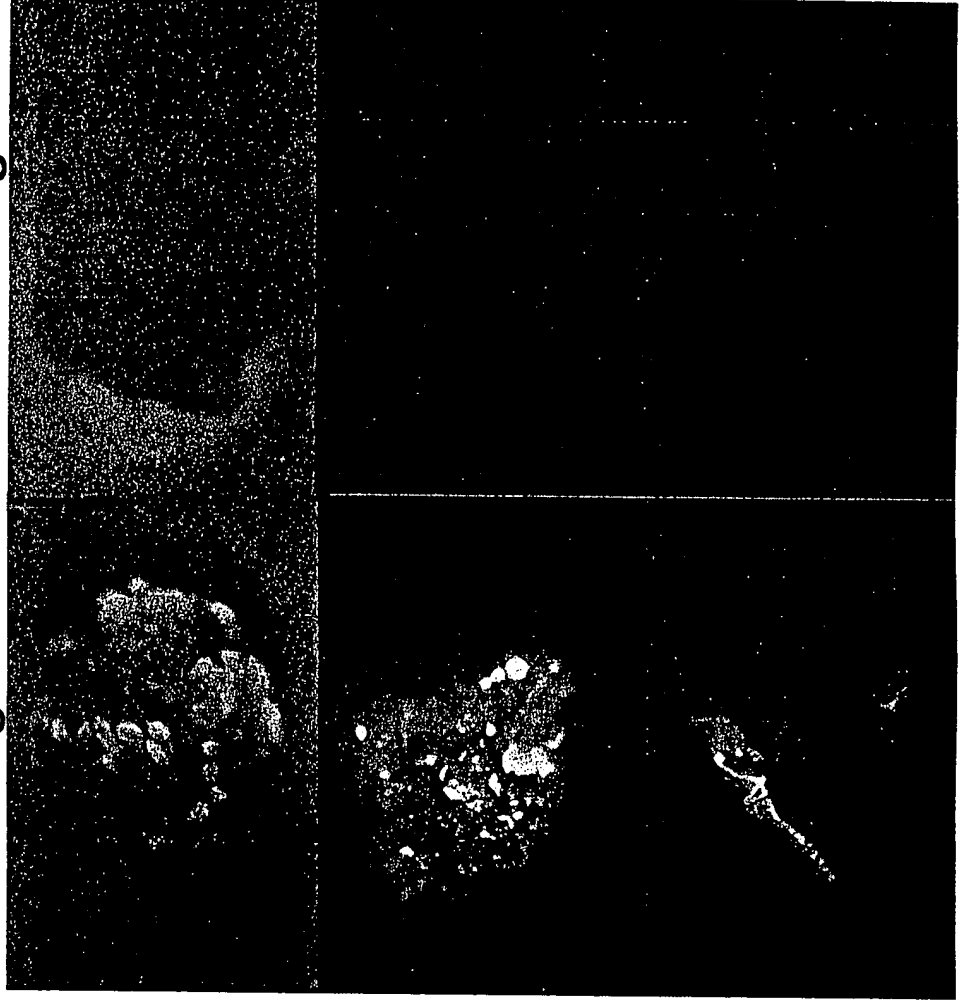


FIGURE 46

550020 3266560

HUMAN

Spleen  
Thymus  
Prostate  
Testis  
Ovary  
S. int.  
Colon  
PBL

Heart  
Brain  
Placenta  
Lung  
Liver  
Muscle  
Kidney  
Panc.

hPSCA →

Northern Analysis

MOUSE

Ant. prostate  
Dorso/Lat. prostate  
Ventral prostate  
Bladder  
Seminal vesicle  
Urethra  
Testis  
Kidney  
Esophagus  
Cardiac stomach  
Body of stomach  
Pyloric stomach  
Duodenum  
Small intestine  
Colon  
Salivary gland  
Spleen  
Thymus  
Bone marrow  
Skeletal muscle  
Heart  
Brain  
Eye  
Lung  
Liver  
Skin

mPSCA →

mG3PDH →

RT-PCR

FIGURE 47

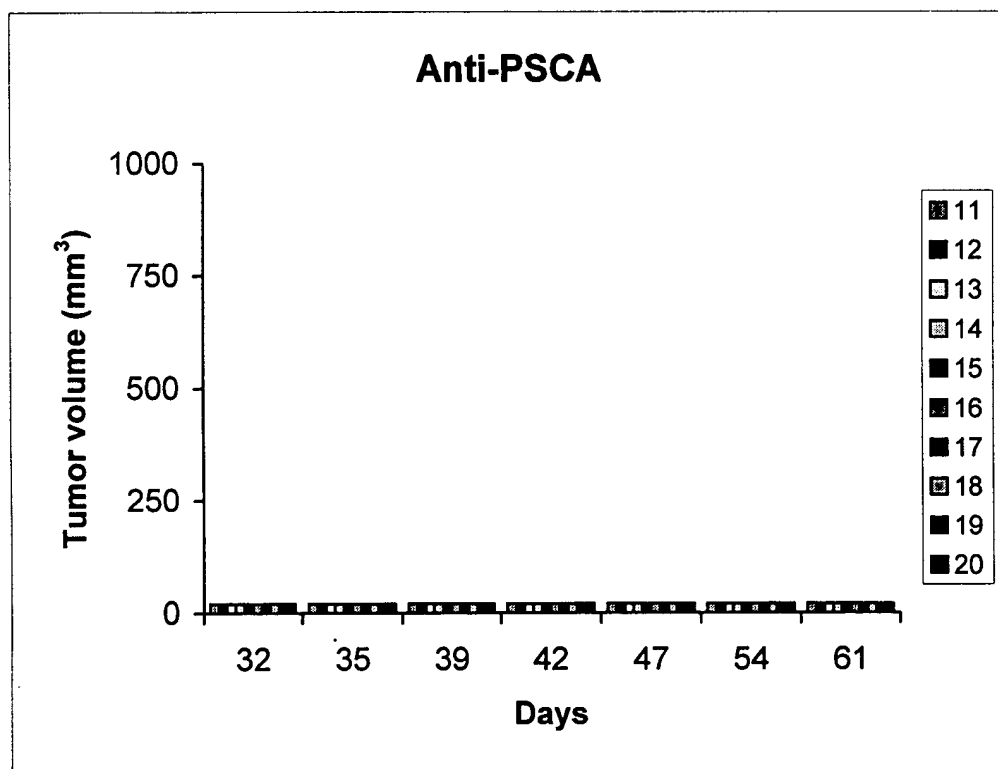
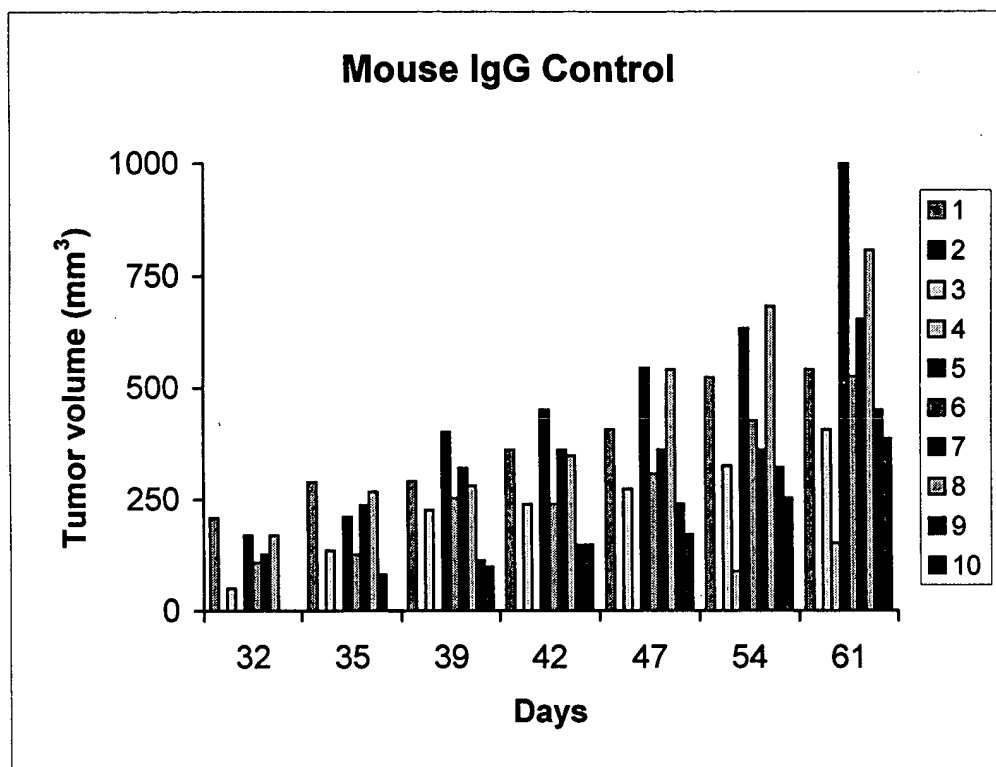


FIG. 49

A

Epitope recognized (OD 450 nm)

mAb	Isotype	F (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1 k	1.485	0.004	1.273	0.003
2A2	IgG2a k	0.973	0.631	0.023	0.010
2H9	IgG1 k	1.069	1.026	0.002	0.001
3C5	IgG2a k	1.916	1.709	0.006	0.002
3E6	IgG3 k	1.609	0.036	1.133	2.118
3G3	IgG2a k	2.805	1.731	0.004	0.000
4A10	IgG2a k	1.053	0.493	0.000	0.001

B

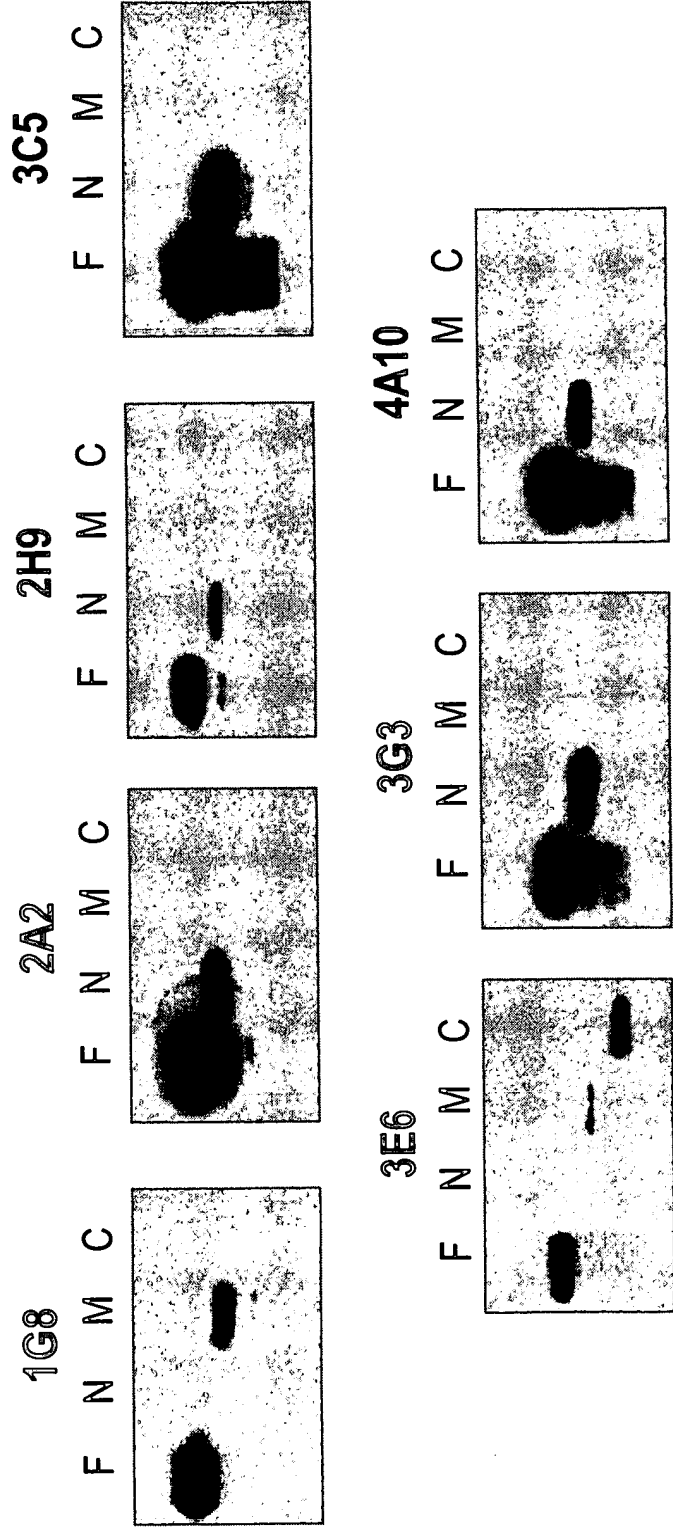
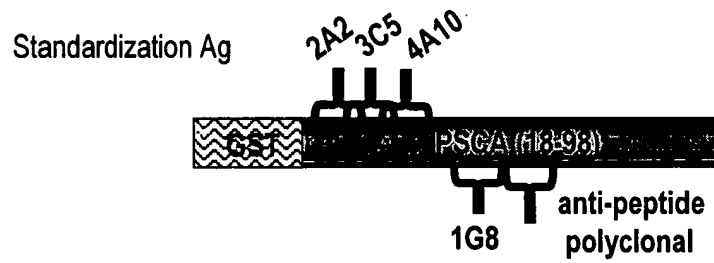


FIG. 50

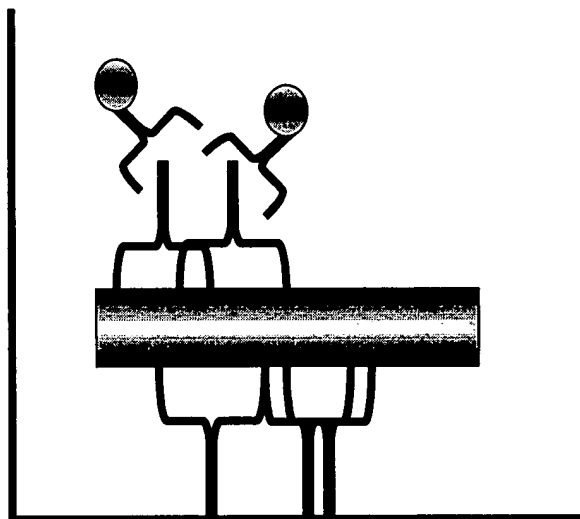
A



Engineered mammalian secreted form



B



Anti-IgG2a HRP

Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)

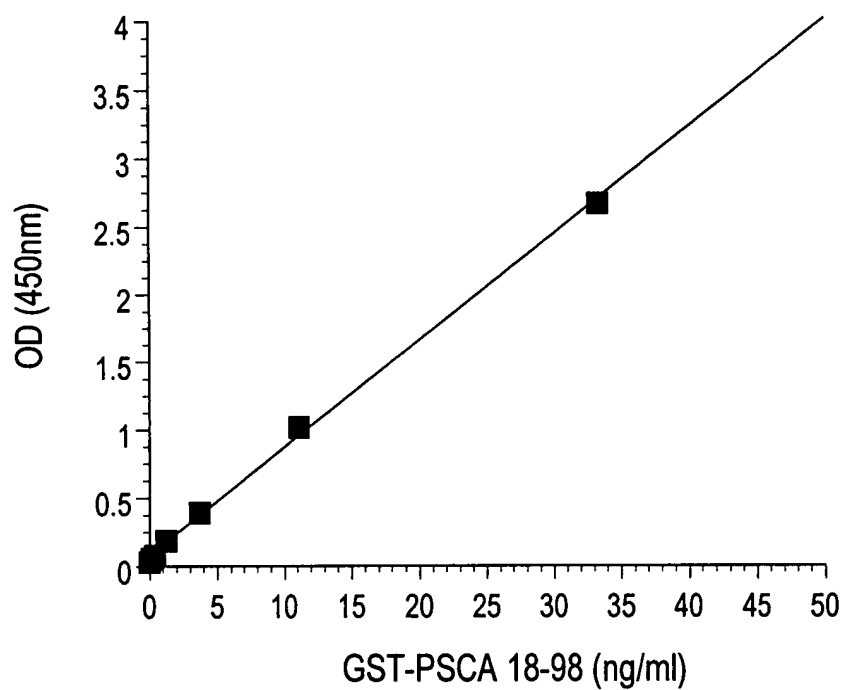
PSCA

Affinity purified anti-peptide polyclonal  
+ mAb 1G8 (IgG1)



FIG. 51

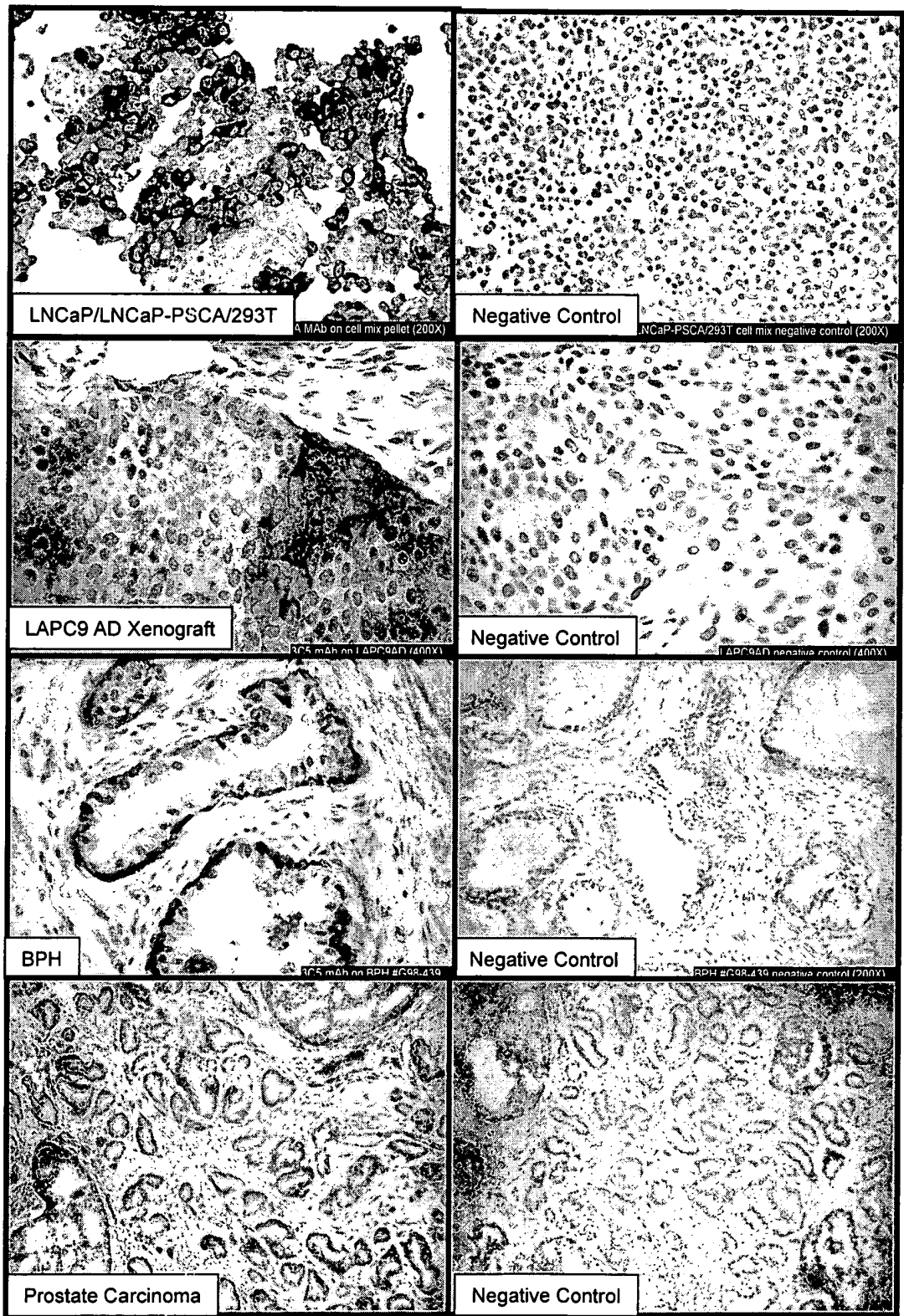
A



B

<u>Sample</u>	<u>OD+range (n=2)</u>	<u>ng/ml</u>
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

FIG. 52



66260" 9263660

FIG. 52

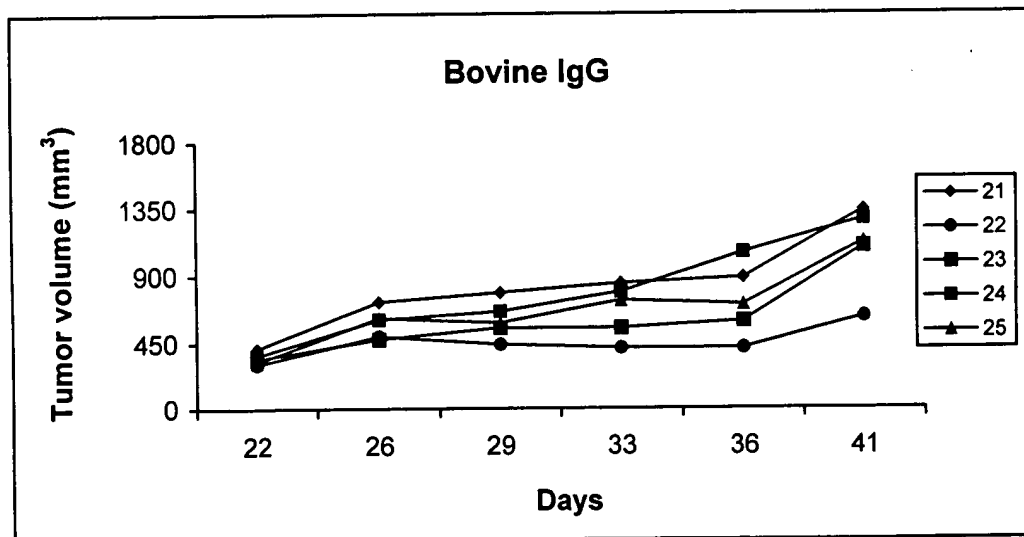
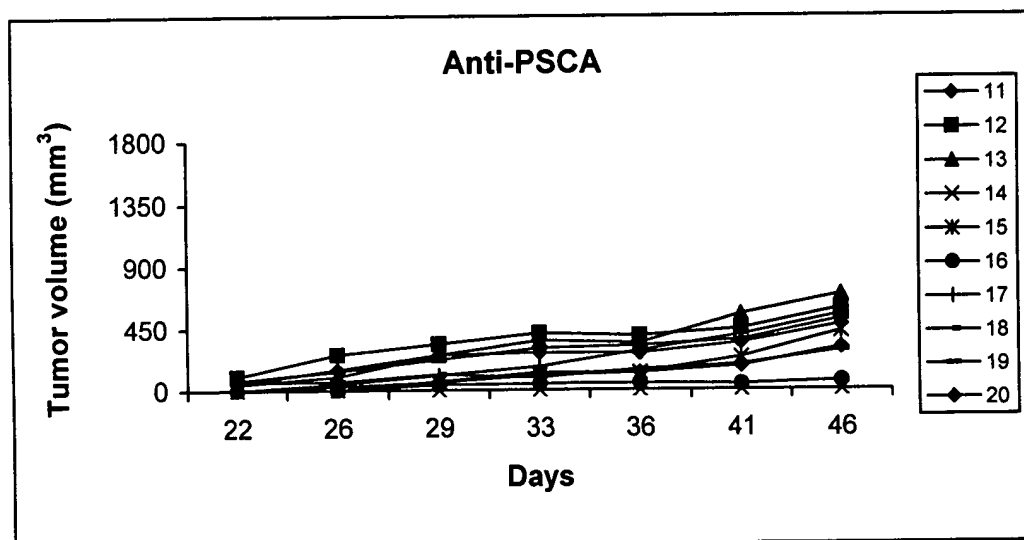
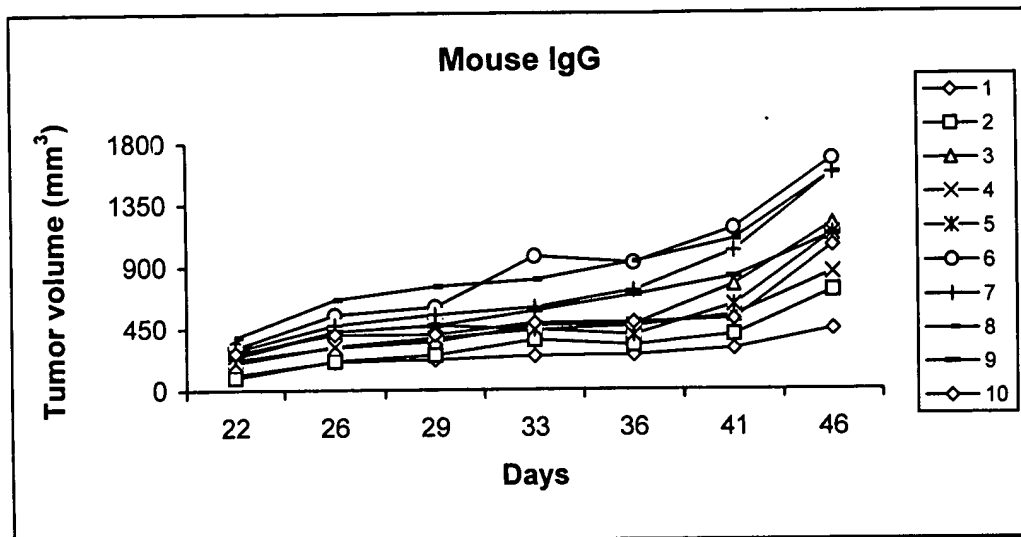


FIG. 54

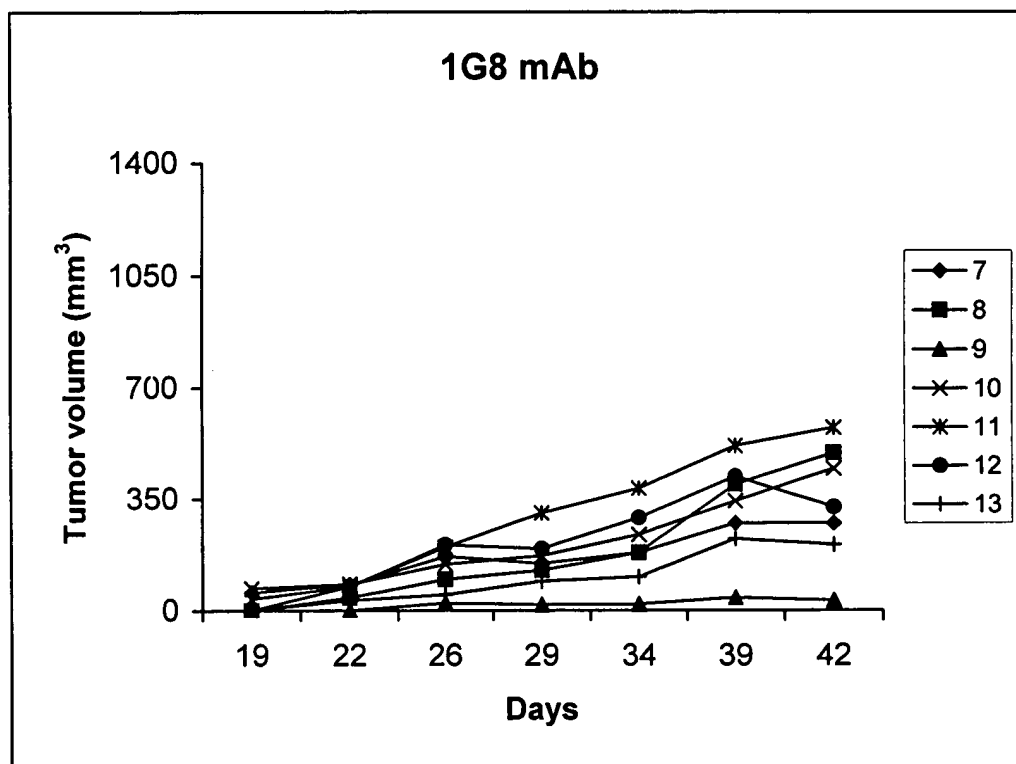
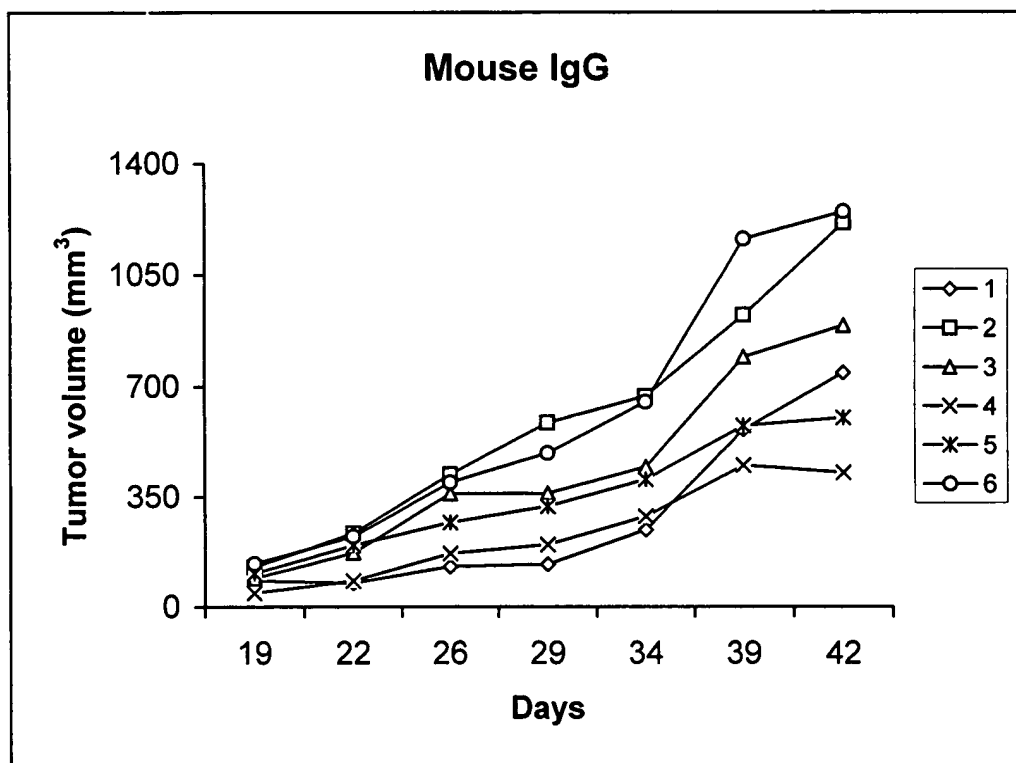


FIG. 55

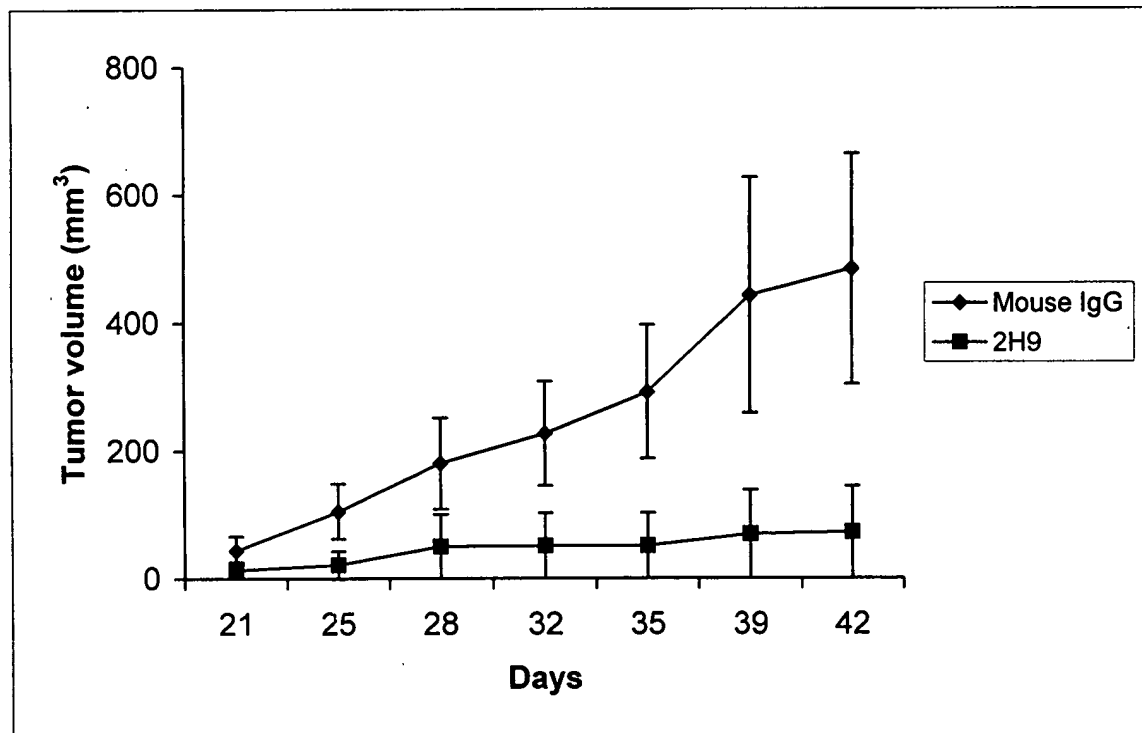
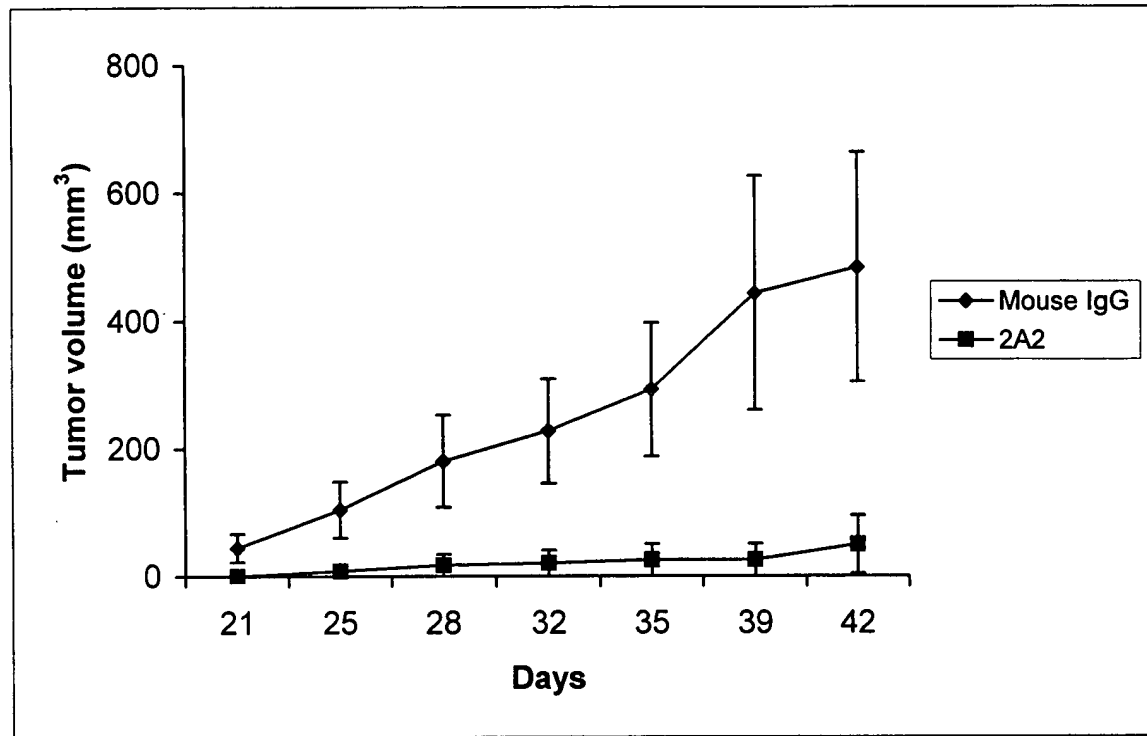


FIG. 56

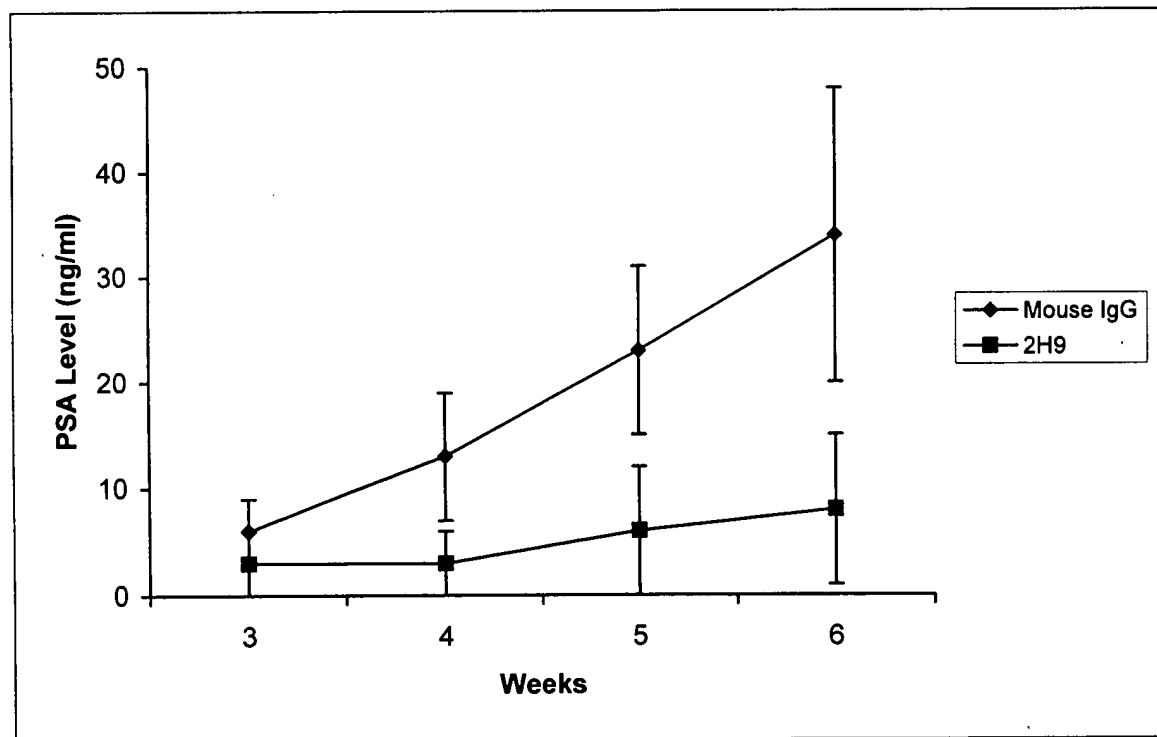
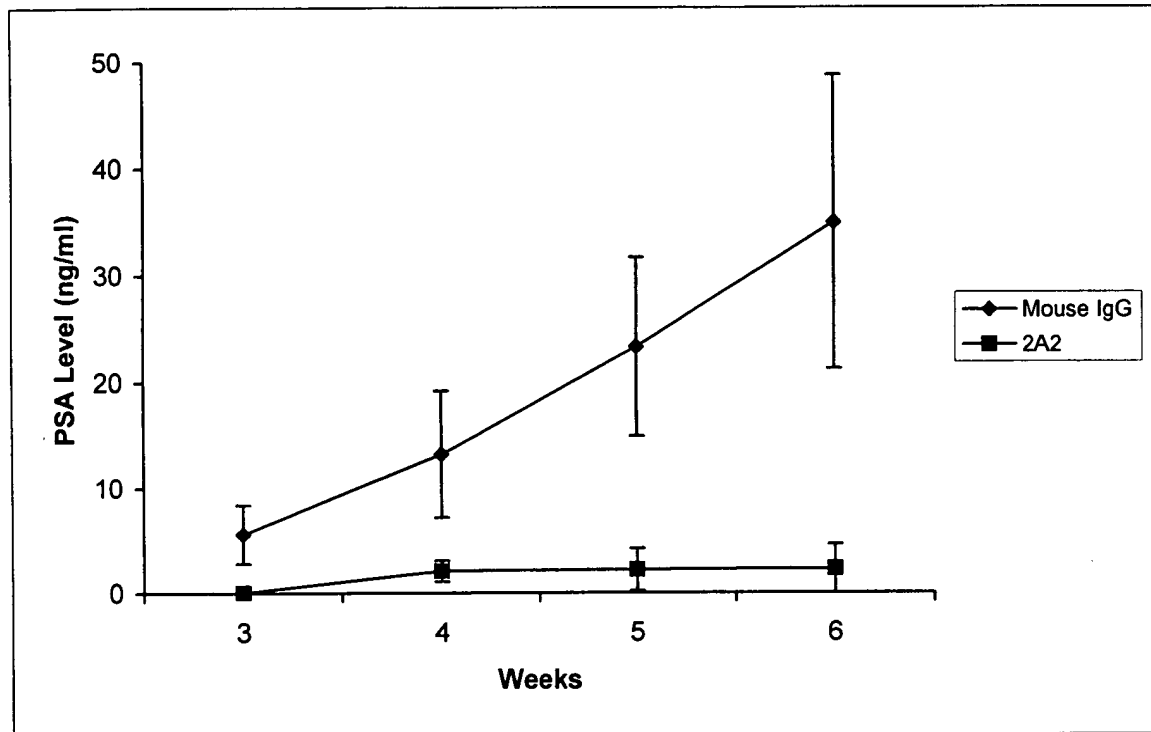


FIG. 57

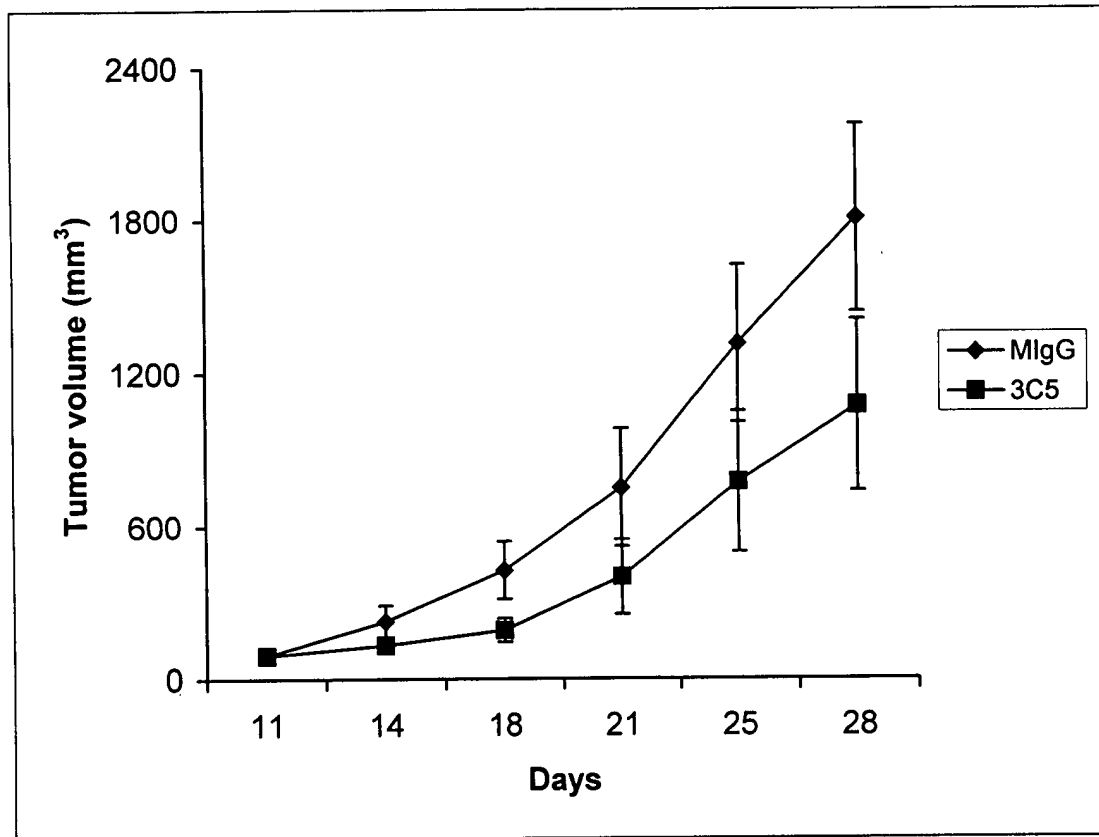


FIG. 58

TGCTTCTTCCTGATGGCAGTGGTTATAGGAGTCAATTCAGAGGTTTCAGCTGCAGCAGTCT 60  
C F F L M A V V I G V N S E V Q L Q Q S 20

GGGGCAGAACTTGTGAGGTCAGGGGCCTCAGTCAAGTTGTCCTGCACAGCTTCTGGCTTC 120  
G A E L V R S G A S V K L S C T A S G F 40

———— CDR1 —————  
AACATTAAAGACTACTATATACACTGGGTGAATCAGAGGCCTGACCAGGGCCTGGAGTGG 180  
N I K D Y Y I H W V N Q R P D Q G L E W 60

———— CDR2 —————  
ATTGGATGGATTGATCCTGAGAATGGTGACACTGAATTTGTCCCGAAGTTCCAGGGCAAG 240  
I G W I D P E N G D T E F V P K F O G K 80

GCCACTATGACTGCAGACATTTTCTCCAACACAGCCTACCTGCACCTCAGCAGCCTGACA 300  
A T M T A D I F S N T A Y L H L S S L T 100

———— CDR3 ————  
TCTGAAGACACTGCCGTCTATTACTGTAAAACGGGGGGTTTCTGGGGCCAAGGGACTCTG 360  
S E D T A V Y Y C K T G G F W G Q G T L 120

GTCACTGTCTCTGCAGCCAAAACGACACCCCCATCTGTCTATCCACTG  
V T V S A A K T T P P S V Y P L

GGGGCAGAACTTGTGAGGTCAGGGGCCTCAGTCAAGTTGTCCTGCACAGCTTCTGGCTTC



FIG. 59

TTGGTAGCAACAGCCTCAGATGTCCACTCCCAGGTCCAAGTGCAGCAACCTGGGTCTGAA 60  
L V A T A S D V H S Q V Q L Q Q P G S E 20

CTGGTGAGGCCTGGAACCTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTATACATTCTCC 120  
L V R P G T S V K L S C K A S G Y T F S 40  
CDR1

AGCTACTGGATGCACTGGGTGAAGCAGAGGCCTGGACAAGGCCTTGAGTGGATTGGAAAT 180  
S Y W M H W V K Q R P G Q G L E W I G N 60

ATTGACCCTGGTAGTGGTTACTACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240  
I D P G S G Y T N Y A E N L K T K A T L 80  
CDR2

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300  
T V D T S S S T A Y M Q L S S L T S E D 100

TCTGCAGTCTATTACTGTACAAGCCGATCTACTATGATTACGACGGGATTGCTTACTGG 360  
S A V Y Y C T S R S T M I T T G F A Y W 120  
CDR3

GGCCAAGGGACTCTGGTCACTGTCTCTGCAGCTACAACAACAGCCCCATCTGTCTATCCA 420  
G Q G T L V T V S A A T T T A P S V Y P 160

CTGGCC  
L A

$\Gamma_{\text{H}}^{(1)}$   $\Gamma_{\text{H}}^{(2)}$   $\Gamma_{\text{H}}^{(3)}$   $\Gamma_{\text{H}}^{(4)}$   $\Gamma_{\text{H}}^{(5)}$   $\Gamma_{\text{H}}^{(6)}$   $\Gamma_{\text{H}}^{(7)}$   $\Gamma_{\text{H}}^{(8)}$   $\Gamma_{\text{H}}^{(9)}$   $\Gamma_{\text{H}}^{(10)}$   $\Gamma_{\text{H}}^{(11)}$   $\Gamma_{\text{H}}^{(12)}$   $\Gamma_{\text{H}}^{(13)}$   $\Gamma_{\text{H}}^{(14)}$   $\Gamma_{\text{H}}^{(15)}$   $\Gamma_{\text{H}}^{(16)}$   $\Gamma_{\text{H}}^{(17)}$   $\Gamma_{\text{H}}^{(18)}$   $\Gamma_{\text{H}}^{(19)}$   $\Gamma_{\text{H}}^{(20)}$   $\Gamma_{\text{H}}^{(21)}$   $\Gamma_{\text{H}}^{(22)}$   $\Gamma_{\text{H}}^{(23)}$   $\Gamma_{\text{H}}^{(24)}$   $\Gamma_{\text{H}}^{(25)}$   $\Gamma_{\text{H}}^{(26)}$   $\Gamma_{\text{H}}^{(27)}$   $\Gamma_{\text{H}}^{(28)}$   $\Gamma_{\text{H}}^{(29)}$   $\Gamma_{\text{H}}^{(30)}$   $\Gamma_{\text{H}}^{(31)}$   $\Gamma_{\text{H}}^{(32)}$   $\Gamma_{\text{H}}^{(33)}$   $\Gamma_{\text{H}}^{(34)}$   $\Gamma_{\text{H}}^{(35)}$   $\Gamma_{\text{H}}^{(36)}$   $\Gamma_{\text{H}}^{(37)}$   $\Gamma_{\text{H}}^{(38)}$   $\Gamma_{\text{H}}^{(39)}$   $\Gamma_{\text{H}}^{(40)}$   $\Gamma_{\text{H}}^{(41)}$   $\Gamma_{\text{H}}^{(42)}$   $\Gamma_{\text{H}}^{(43)}$   $\Gamma_{\text{H}}^{(44)}$   $\Gamma_{\text{H}}^{(45)}$   $\Gamma_{\text{H}}^{(46)}$   $\Gamma_{\text{H}}^{(47)}$   $\Gamma_{\text{H}}^{(48)}$   $\Gamma_{\text{H}}^{(49)}$   $\Gamma_{\text{H}}^{(50)}$   $\Gamma_{\text{H}}^{(51)}$   $\Gamma_{\text{H}}^{(52)}$   $\Gamma_{\text{H}}^{(53)}$   $\Gamma_{\text{H}}^{(54)}$   $\Gamma_{\text{H}}^{(55)}$   $\Gamma_{\text{H}}^{(56)}$   $\Gamma_{\text{H}}^{(57)}$   $\Gamma_{\text{H}}^{(58)}$   $\Gamma_{\text{H}}^{(59)}$   $\Gamma_{\text{H}}^{(60)}$   $\Gamma_{\text{H}}^{(61)}$   $\Gamma_{\text{H}}^{(62)}$   $\Gamma_{\text{H}}^{(63)}$   $\Gamma_{\text{H}}^{(64)}$   $\Gamma_{\text{H}}^{(65)}$   $\Gamma_{\text{H}}^{(66)}$   $\Gamma_{\text{H}}^{(67)}$   $\Gamma_{\text{H}}^{(68)}$   $\Gamma_{\text{H}}^{(69)}$   $\Gamma_{\text{H}}^{(70)}$   $\Gamma_{\text{H}}^{(71)}$   $\Gamma_{\text{H}}^{(72)}$   $\Gamma_{\text{H}}^{(73)}$   $\Gamma_{\text{H}}^{(74)}$   $\Gamma_{\text{H}}^{(75)}$   $\Gamma_{\text{H}}^{(76)}$   $\Gamma_{\text{H}}^{(77)}$   $\Gamma_{\text{H}}^{(78)}$   $\Gamma_{\text{H}}^{(79)}$   $\Gamma_{\text{H}}^{(80)}$   $\Gamma_{\text{H}}^{(81)}$   $\Gamma_{\text{H}}^{(82)}$   $\Gamma_{\text{H}}^{(83)}$   $\Gamma_{\text{H}}^{(84)}$   $\Gamma_{\text{H}}^{(85)}$   $\Gamma_{\text{H}}^{(86)}$   $\Gamma_{\text{H}}^{(87)}$   $\Gamma_{\text{H}}^{(88)}$   $\Gamma_{\text{H}}^{(89)}$   $\Gamma_{\text{H}}^{(90)}$   $\Gamma_{\text{H}}^{(91)}$   $\Gamma_{\text{H}}^{(92)}$   $\Gamma_{\text{H}}^{(93)}$   $\Gamma_{\text{H}}^{(94)}$   $\Gamma_{\text{H}}^{(95)}$   $\Gamma_{\text{H}}^{(96)}$   $\Gamma_{\text{H}}^{(97)}$   $\Gamma_{\text{H}}^{(98)}$   $\Gamma_{\text{H}}^{(99)}$   $\Gamma_{\text{H}}^{(100)}$

CCCCATCTGTCTATCCACTGGCCCCTTGTGTA  
P P S V Y P L A P C V

# FIG. 61

## CDR1 Comparisons

1G8	1gG <sub>1k</sub>	Middle	G	F	N	I	K	D	Y	Y	I	H
2H9	1gG <sub>1k</sub>	N-Term.	G	F	T	F	S	N	Y	W	M	T
4A10	1gG <sub>2ak</sub>	N-Term.	G	Y	T	F	S	S	Y	W	M	H

## CDR2 Comparisons

1G8	1gG <sub>1k</sub>	W	I	D	P	E	N	G	D	T	E	F	V	P	K	F	Q	G		
2H9	1gG <sub>1k</sub>	E	I	R	L	R	S	E	N	Y	A	T	H	Y	A	E	S	V	K	G
4A10	1gG <sub>2ak</sub>	N	I	D	P	G	S	G	Y	T	N			Y	A	E	N	L	K	T

## CDR3 Comparisons

1G8	1gG <sub>1k</sub>	G	G	F													
2H9	1gG <sub>1k</sub>	L	G	R	P	N											
4A10	1gG <sub>2ak</sub>	R	S	T	M	I	T	T	G	F	A	Y					

003536 035360 003536 035360

FIG. 62

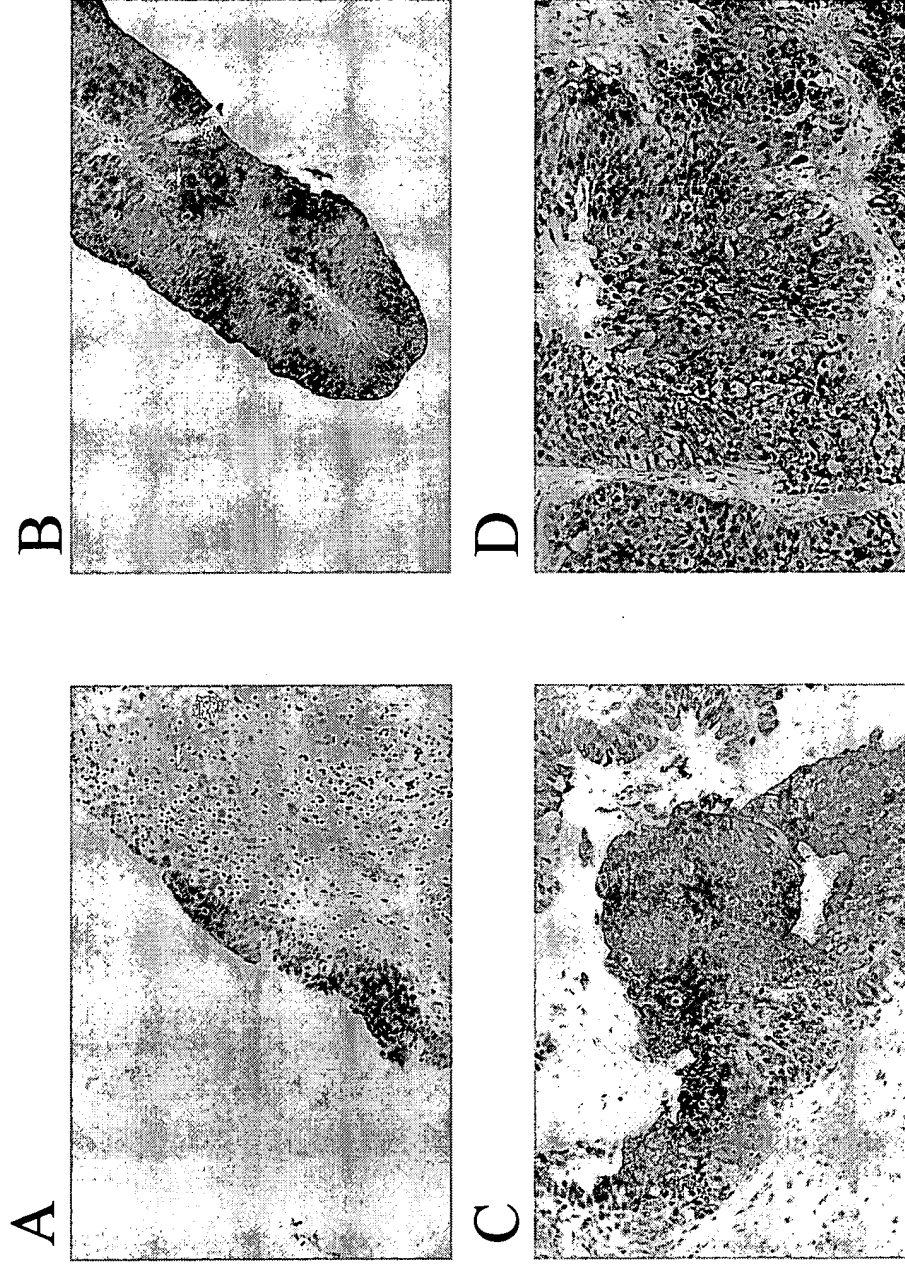


FIG. 63

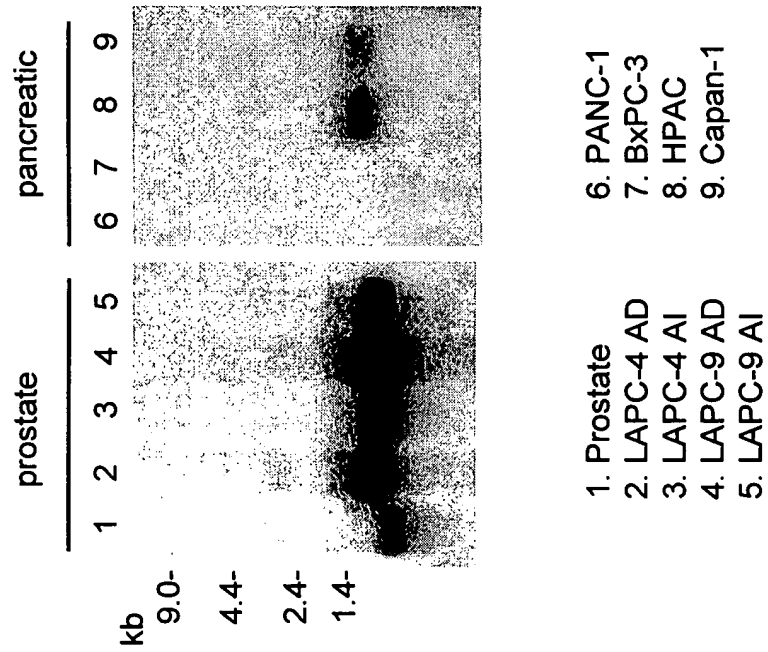
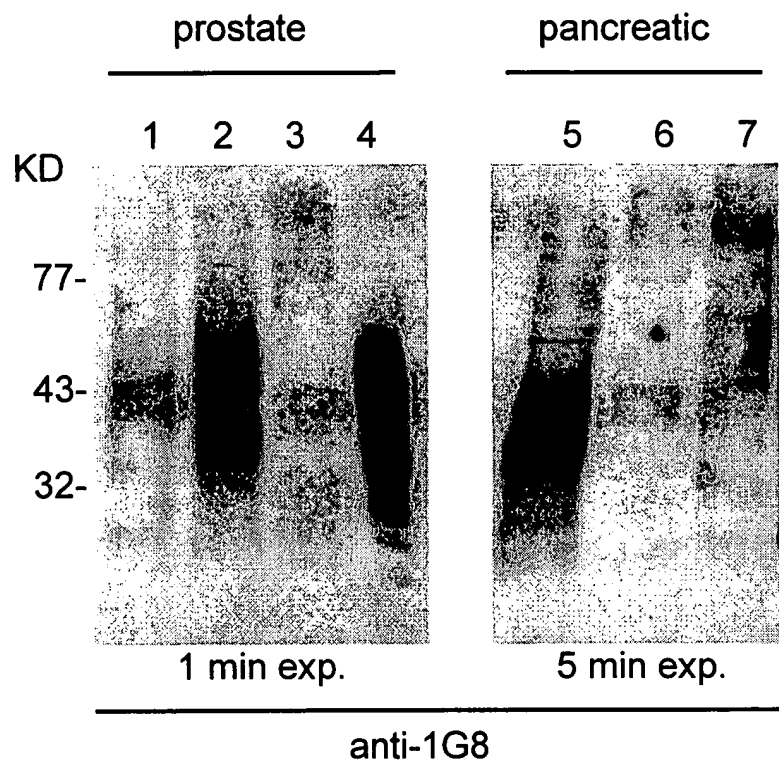


FIG. 64



- 1. LAPC-4 AD
- 2. LAPC-9 AI
- 3. LNCaP
- 4. LNCaP-PSCA
- 5. HPAC
- 6. Capan-1
- 7. ASPC-1

66020-36960

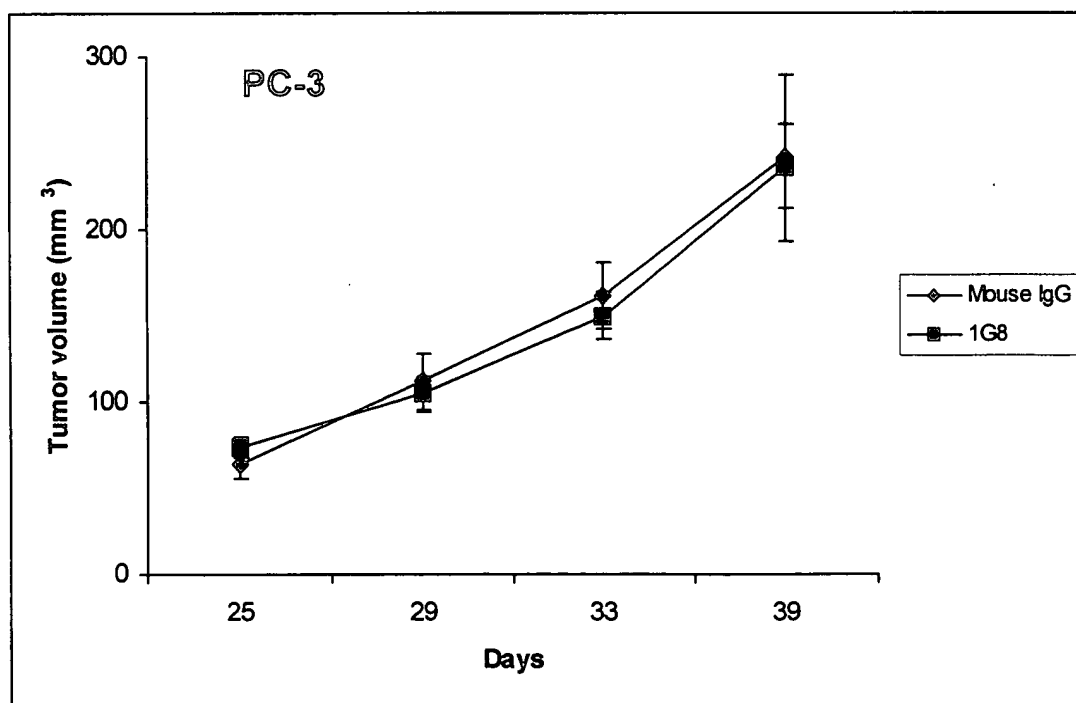
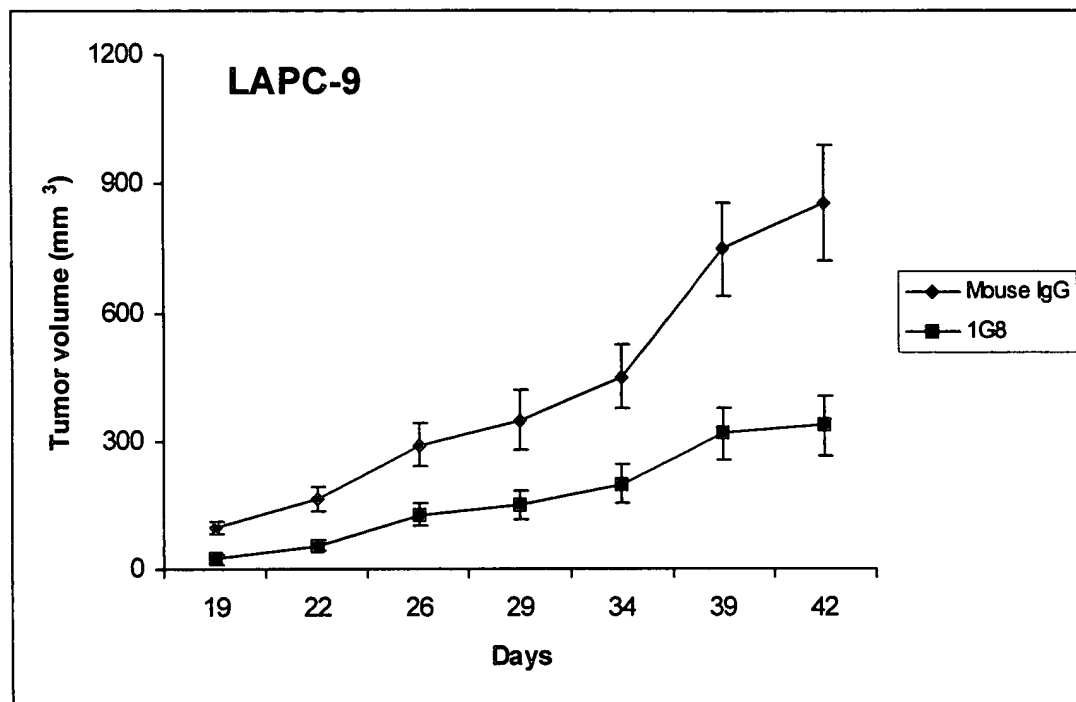


FIGURE 65